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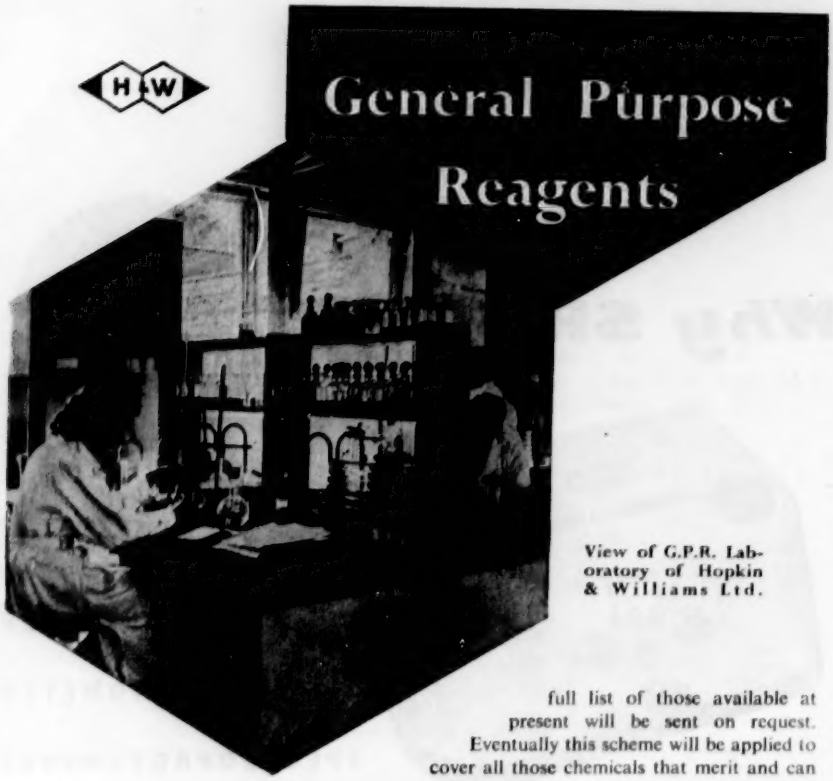

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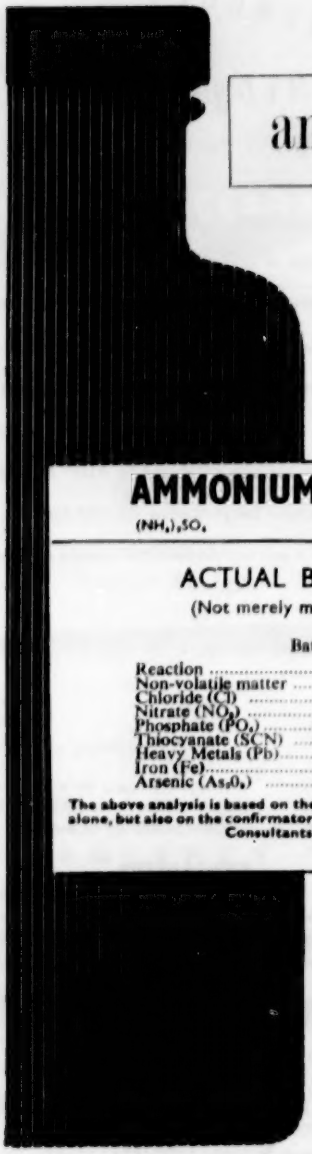

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JOURNAL
OF
THE CHEMICAL SOCIETY

1. *The Reaction of* o-*Di-iodobenzene with Magnesium, Lithium, and* n-*Butyl-lithium.*

By Harry Heaney, Frederick G. Mann, and Ian T. Millar.

The reaction of *o*-di-iodobenzene with the above reagents, followed by carboxylation of the product, has been investigated. The main product isolated with magnesium is diphenyl, and with lithium is tri-*o*-phenylene. *n*-Butyl-lithium affords a mixture of 2 : 2′-di-(*o*-carboxyphenyl)diphenyl and 2 : 2′-di-(*o*-*n*-butylphenyl)diphenyl. The origin of these products is briefly discussed.

p-Dibromobenzene with magnesium under suitable conditions gives a mono- or a di-magnesium derivative (Ziegler and Tiemann, *Ber.*, 1922, **55**, 3406; Gilman, Beaber, and Jones, *Rec. Trav. chim.*, 1929, **48**, 597; von Braun, Irmisch, and Nelles, *Ber.*, 1933, **66**, 1471): 1 : 4-dibromonaphthalene behaves similarly (Zalkind, *Ber.*, 1934, **67**, 1031). *p*-Dibromobenzene can also be converted into *p*-bromophenyl-lithium by the action of *n*-butyl-lithium (Gilman and Melvin, *J. Amer. Chem. Soc.*, 1950, **72**, 995).

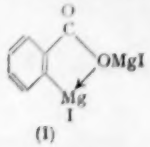
The preparation of *o*-phenylenebis(magnesium halide) or of *o*-phenylenedilithium would be of great value, particularly for the synthesis of cyclic systems, and we have therefore studied the action of magnesium, lithium, and *n*-butyl-lithium on *o*-di-iodobenzene in particular.

The reaction of magnesium with the three di-iodobenzenes, first noted by Votoček and Kohler (*Ber.*, 1914, **47**, 1219), was further investigated by Bruhat and Thomas (*Compt. rend.*, 1926, **183**, 297) who found that all three di-iodobenzenes react with substantially more than one equivalent of magnesium, and that the product from the *meta*- and the *para*-compound on carboxylation gave *iso*phthalic and terephthalic acid in 15 and 50% yield respectively, whereas that from the *ortho*-compound gave only benzoic acid in unspecified yield. They concluded that all the di-iodobenzenes give the corresponding phenylenebis-(magnesium iodide), and confirmed this process for the *ortho*-derivative by treating the product with benzonitrile and with benzophenone, subsequently isolating the expected diketone and glycol respectively, in low yield.

We found that *o*-di-iodobenzene in ether reacted readily with 1 equivalent of magnesium, and the product, when carboxylated in the usual way, afforded *o*-iodobenzoic acid (29%), unchanged di-iodobenzene (25%), and a trace of benzoic acid. The use of 2 equivalents of magnesium also gave a vigorous reaction, but even after prolonged digestion only 1·5 equivalents had reacted: carboxylation then gave benzoic acid (5·5% after purification), no other acid being detected, while the ether layer afforded diphenyl (17%).

These results, we suggest, indicate that some *o*-phenylenebis(magnesium iodide) is formed, but that it reacts with carbon dioxide to give the complex (I), which resists further carboxylation and on hydrolysis forms benzoic acid. The major reaction arises almost undoubtedly by an initial Fittig condensation, giving 2 : 2′-di-iododiphenyl, which then forms the bis(magnesium iodide) derivative (II), hydrolysis of which gives the diphenyl. This mechanism is supported by the fact that under the conditions employed by us and by Bruhat and Thomas (*loc. cit.*), the *o*-di-iodobenzene could not be induced to react with more than 1·5—1·6 equivalents of magnesium. The lack of reactivity of the derivative (II) with carbon dioxide may be due partly to steric hindrance, but also to the very low solubility

of this di-Grignard reagent in ether and in benzene. The product of the interaction of *o*-di-iodobenzene with an excess of magnesium was therefore treated with the more reactive iododimethylarsine; this yielded 2-diphenylyldimethylarsine (58%, characterised as the methiodide) and unchanged iodoarsine (16%), but no *o*-phenylenebis(dimethylarsine) could be detected. Here again it is probable that the initial reaction of the iodoarsine on the Grignard reagent (II) is to produce the stable co-ordinated arsine derivative (III), which on hydrolysis yields 2-diphenylyldimethylarsine.



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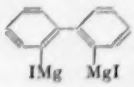

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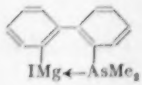

(III)

The use of lithium and then of *n*-butyl-lithium gave progressively more complex products. *o*-Di-iodobenzene reacted readily with lithium (4·1 equivalents) but the product on carboxylation gave no acids; the ether layer, however, yielded tri-*o*-phenylene (IV) in 30% yield. This reaction affords a ready method of preparing this hydrocarbon in the pure state.

o-Di-iodobenzene reacted smoothly with *n*-butyl-lithium and the product on carboxylation gave 2 : 2′-di-(*o*-carboxyphenyl)diphenyl (V; R = CO_2H) (17%), and the ether layer afforded 2 : 2′-di-(*o*-*n*-butylphenyl)diphenyl (V; R = Bu^n) (5%); these yields (as in the other experiments) are certainly low owing to loss incurred in both isolation and purification of the products.

(IV)

(V)

The reasons for this striking difference in the action of lithium and *n*-butyl-lithium, and the sequence of reactions leading ultimately to the triphenylene and the quaterphenyl system respectively, are at present unknown. Consideration of three known factors, (*a*) the reaction of magnesium or lithium with more than one halogen atom in a di- or poly-halogenobenzene never occurs readily, and often not at all (Gilman, Beaber, and Jones, *loc. cit.*; Gilman, Zoellner, and Selby, *J. Amer. Chem. Soc.*, 1933, **55**, 1252; Votoček and Kohler, *loc. cit.*), (*b*) *n*-butyl-lithium is generally more reactive than metallic lithium in replacing aromatic halogen by lithium (Gilman and Jones, "Organic Reactions," Vol. VI, p. 339, Wiley, New York, 1951), (*c*) 2 : 2′-di-iododiphenyl readily reacts with lithium to give 2 : 2′-dilithiodiphenyl (Wittig and Geissler, *Annalen*, 1953, **580**, 44), suggests that, of the several routes by which the above systems might arise, the following appear the most probable. With both reagents, the initial major reaction is the formation in turn of 2 : 2′-di-iodo- and 2 : 2′-dilithio-diphenyl. In the heterogeneous conditions of the comparatively slow lithium reaction, some *o*-di-iodobenzene might still be present at this stage and would have opportunity to react with the dilithiodiphenyl to give triphenylene (IV). The far more rapid *n*-butyl-lithium reaction in a homogeneous solution would almost certainly ensure that at this stage any di-iodobenzene not already involved in the formation of 2 : 2′dilithiodiphenyl would be converted into *o*-lithio-iodobenzene, and the interaction of these compounds would give the quaterphenyl system. The 2 : 2′-di-(*o*-*n*-butylphenyl)-diphenyl (V; R = Bu^n) clearly might arise from the butylation of a portion either of the intermediate *o*-lithio-iodobenzene as a competing reaction or of the final 2 : 2′-di-(*o*-lithiophenyl)diphenyl.

o-Dibromobenzene could not be induced to react directly with magnesium. It reacted in ethereal solution with lithium only on prolonged boiling to give a yellowish-brown amorphous solid, m. p. 280—285°, which could not be satisfactorily purified. This product is possibly identical with the yellow amorphous powder, m. p. 280—290°, which Hosaeus

(*Monatsh.*, 1893, **14**, 323) obtained by the action of sodium in similar conditions. *o*-Dibromobenzene with *n*-butyl-lithium gave a small quantity of the hydrocarbon (V; R = Bu^n) and, as the main product, a colourless amorphous solid, melting above 350° and insoluble in all common solvents; this solid was not further investigated.

Although an intensive investigation of the above reactions, with considerable variation in the many factors involved, might well reveal a change in the yield and even the nature of the products, it is clear that the preparation of an *o*-phenylenebis(magnesium halide) or of *o*-phenylene-dilithium as a synthetic reagent is not practicable under the conditions described above.

Experimental

Experiments with metals and with *n*-butyl-lithium were performed in a nitrogen atmosphere. Carboxylation was carried out by pouring the reaction solution into a slurry of solid carbon dioxide and ether. In all experiments the non-acidic product was carefully examined for the presence of 2 : 2′-di-iododiphenyl, and also (except in experiments involving benzene as a solvent) benzene : neither compound was detected.

Reactions with Magnesium.—(*a*) A solution of *o*-di-iodobenzene (9·9 g.) in ether (50 c.c.) was added dropwise to a stirred mixture of magnesium (0·73 g., 1 atom) and ether (10 c.c.), which reacted readily, external cooling being required. The mixture was then stirred at room temperature for 2 hr., and the clear yellow solution, containing no free magnesium, was carboxylated. The product was extracted with aqueous sodium hydroxide, which when acidified deposited a crude crystalline acid : distillation of this acid in steam gave a trace of benzoic acid; the remainder, when recrystallised from water, afforded *o*-iodobenzoic acid (2·2 g., 29%; m. p. 160°; *p*-bromophenacyl ester, m. p. 110°). The ether layer on evaporation gave *o*-di-iodobenzene, b. p. 78—82°/0·05 mm. (2·5 g., 25%).

(*b*) The above experiment was repeated but with magnesium (1·46 g., 2 atoms), the ethereal *o*-di-iodobenzene being added at such a rate that the mixture did not boil. The Grignard reagent separated as a heavy amber-coloured oil. The mixture was stirred for 3 hr. at room temperature, filtered to remove unchanged magnesium (0·37 g., 0·5 atom), and carboxylated. The mixture was acidified with dilute hydrochloric acid, then basified and extracted with aqueous sodium hydroxide. The latter when acidified deposited a crude acid, m. p. 114°, which when recrystallised thrice from light petroleum (b. p. 60—80°) and twice from water afforded benzoic acid (0·2 g., 5·5%), m. p. alone and mixed, 120°. The ethereal layer, when dried and distilled, gave diphenyl, b. p. 140—160°/15 mm., m. p. alone and mixed, 67° after recrystallisation from methanol (0·4 g., 17%).

(*c*) A Grignard reagent was prepared from *o*-di-iodobenzene (16·5 g.) in ether (70 c.c.) and magnesium (1·95 g., 1·6 atoms), benzene (20 c.c.) being then added to give a homogeneous solution with only a trace of undissolved magnesium. The solution was stirred for 2 hr., and then cooled in ice-water whilst iododimethylarsine (18·6 g., 1·6 mols.) in benzene (30 c.c.) was slowly added. The clear yellow solution was boiled under reflux for 2 hr., cooled in ice, and hydrolysed with aqueous ammonium chloride. The organic layer, when dried and distilled, gave iododimethylarsine, b. p. 30—50°/0·3 mm. (3 g., 16%), and 2-diphenylyldimethylarsine, b. p. 98—110°/0·3 mm. (6·5 g.). The latter product on treatment with methyl iodide gave *2-diphenylyltrimethylarsonium iodide* (4·6 g., 58%), m. p. 259—260° (from ethanol) (Found : C, 44·8; H, 5·0. $C_{15}H_{18}IAs$ requires C, 45·0; H, 4·55%).

To confirm the identity of the tertiary arsine, a Grignard reagent was prepared under nitrogen from 2-iododiphenyl (14 g.) and magnesium (1·3 g., 1·06 atoms) in ether (70 c.c.), into which, after 90 minutes' stirring at room temperature, a solution of iododimethylarsine (11·6 g., 1 mol.) in benzene (40 c.c.) was added during 15 min. The mixture was boiled under reflux for 2 hr., cooled in ice, and hydrolysed as before. The organic layer, when dried and distilled, gave 2-diphenylyldimethylarsine, b. p. 104—106°/0·3 mm. (6 g., 46%). This gave a methiodide, which, after crystallisation from ethanol, had m. p. 259—260°, undepressed by admixture with the above iodide. The arsine, prepared in this way, gives high carbon values on analysis, owing to contamination with diphenyl, with which it co-distils. The methiodide was therefore decomposed by being heated under nitrogen at 280°/0·15 mm.; the distillate on refractionation gave the pure *arsine*, b. p. 114°/0·5 mm. (Found : C, 65·1; H, 5·7. $C_{14}H_{15}As$ requires C, 65·1; H, 5·9%).

It is noteworthy that a repetition of experiment (*c*), but with chlorodiphenylarsine, gave a product from which only iododiphenylarsine, b. p. 137—139°/0·4 mm., was isolated.

Reaction with Lithium.—A solution of *o*-di-iodobenzene (6·6 g.) in ether (20 c.c.) was added dropwise to a stirred mixture of fine lithium foil (0·6 g., 4·1 atoms) in ether during 3 hr., reaction readily occurring. Benzene (25 c.c.) was then added and the mixture boiled under reflux for 3 hr. Carboxylation of the cooled product gave no trace of an organic acid. The organic layer, when dried and evaporated, gave a dark solid residue, which after crystallisation from ethanol (charcoal) followed by sublimation at 160—180°/0·4 mm., afforded tri-*o*-phenylene (IV) (0·45 g., 30%), m. p. 191—192° (Found: C, 95·0; H, 5·6. Calc. for $C_{18}H_{12}$: C, 94·7; H, 5·3%). The identity of this hydrocarbon was confirmed by its ultraviolet absorption spectrum in ethanol, which gave the characteristic maxima (with $\log_{10}\varepsilon$ values in parentheses): 249 (4·95), 258 (5·2), 273 (4·3), 285 (4·25), 315 (3·2), 327 (3·0), 333 mμ (3·15): these values accord closely with those given by Clar and Lombardi (*Ber.*, 1932, **65**, 1411; cf. also Rapson, Schwartz, and Stewart, *J.*, 1944, 73).

In an experiment similar to the above but with *o*-dibromobenzene, the boiling under reflux was continued for 12 hr. before the lithium was extensively attacked. Carboxylation gave no trace of acid, and no triphenylene was detected in the ethereal layer. The latter on evaporation gave a dark non-volatile residue which was extracted with cold benzene. Dilution of the extract with ethanol gave a yellow-brown amorphous precipitate, m. p. 280—285° after three reprecipitations. In view of the nature of the product and its difficult purification, it was not further investigated.

Reaction with n-*Butyl-lithium.*—A solution of *o*-di-iodobenzene (6·6 g.) in benzene (50 c.c.) and light petroleum (b. p. 40—60°) (100 c.c.) was added to a stirred 1·91N-solution of *n*-butyl-lithium (26 c.c., 2·4 mols. of solute) in the above petroleum, a vigorous exothermic reaction rapidly developing. The mixture was boiled under reflux for 3 hr., and then carboxylated. Working up in the usual way gave an acid (0·6 g.) and a hydrocarbon (0·15 g.), both colourless crystalline compounds.

Recrystallisation of the acid from ethanolic petroleum or from aqueous ethanol gave 2 : 2′-*di*-(*o-carboxyphenyl*)*diphenyl* (V; R = CO_2H) (0·35 g., 17%), which retained ethanol even after drying at 80°/0·2 mm. for 6 hr. (Found: C, 78·4; H, 5·0. $C_{26}H_{18}O_4,0{\cdot}25C_2H_6O$ requires C, 78·4; H, 4·85%), but which on sublimation at 200—220°/0·1 mm. gave the pure acid, m. p. 244—245° (Found: C, 79·0; H, 4·8%; *M*, ebullioscopic in ethanol, 408. $C_{26}H_{18}O_4$ requires C, 79·15; H, 4·6%; *M*, 394). A methanolic solution of the acid, when saturated with hydrogen chloride and boiled for 1 hr., gave the *dimethyl ester*, m. p. 147—148°, after crystallisation from light petroleum (b. p. 60—80°) (Found: C, 79·75; H, 5·1. $C_{28}H_{22}O_4$ requires C, 79·6; H, 5·25%). The infrared spectrum of the acid (V; R = CO_2H), determined in a hexachlorobutadiene mull, showed bands at 6·24, 6·35, 13·30, and 13·40 μ, assigned to the *o*-phenylene groups, and at 5·92 and 10·7 μ, assigned to the CO_2H groups.

The hydrocarbon, recrystallised from ethanolic benzene, gave 2 : 2′-*di*-(o-n-*butylphenyl*)-*diphenyl* (V; R = Bu^n) (0·10 g., 5%), m. p. 228—230° raised to 229—231° by sublimation at 260—270°/0·1 mm. (Found: C, 92·0; H, 7·6%; *M*, ebullioscopic in carbon tetrachloride, 413. $C_{32}H_{34}$ requires C, 91·8; H, 8·2%; *M*, 419). The infrared spectrum, determined as above, showed bands at 6·25, 13·28, and 13·41 μ due to the *o*-phenylene groups, at 3·43 and 3·51 μ due to the CH_2 groups, and at 7·27 μ assigned to the ·C·Me group. The ultraviolet spectrum (solution in light petroleum, b. p. 60—80°) showed no maximum or minimum over the range 200—300 mμ. The identity of the hydrocarbon is confirmed by the very close similarity of this spectrum with that of 2 : 2′-diphenyldiphenyl (V; R = H) in ethanol and *n*-hexane determined by Rapson, Schwartz, and Stewart (*loc. cit.*): the following values for this compound have been measured from the very small curve given by these authors.

(V; R = Bu^s)	λ (mμ)	210	245	250	257	270
	$\log_{10}\varepsilon$	4·35	4·00	3·93	3·85	3·70
(V; R = H)	λ (mμ)	210	245	250	257	270
	$\log_{10}\varepsilon$	4·6	4·3	4·25	4·1	3·75

o-Di-iodobenzene was also treated with *n*-butyl-lithium (1 mol.) in the petroleum solution at 0° for 1 min., and the product was then carboxylated; working up as before gave the acid (V; R = CO_2H) in lower yield, with a trace of benzoic acid and some unchanged *o*-di-iodobenzene.

o-Dibromobenzene, when similarly treated with *n*-butyl-lithium (2·4 mols.), gave as the main product a colourless solid, which was insoluble in all common organic solvents and did not melt below 350°; the crude material, when extracted with boiling ethanol, gave the hydrocarbon (V; R = Bu^n) in very low yield. No acid could be isolated from the products of

carboxylation. *o*-Dibromobenzene, when treated with *n*-butyl-lithium (1 mol.) in the petroleum at 0° for 5 min. and then carboxylated, gave the same products, *o*-dibromobenzene (75%) being recovered unchanged.

We are indebted to Trinity College, Cambridge, for a Senior Rouse Ball Studentship (to I. T. M.), and to the University College of North Staffordshire for a Tutorial Studentship (to H. H.).

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KEELE, STAFFORDSHIRE. [*Received, August 4th*, 1955.]

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2. *The Effect of Solvents on the Molecular Complexities of Tantalum* n-*Alkoxides.*

By D. C. BRADLEY, W. WARDLAW, and (MISS) ALICE WHITLEY.

The molecular weights of tantalum alkoxides $Ta(OR)_5$, where R = Me, Et, Pr^n, or Bu^n, have been determined ebullioscopically in toluene, acetonitrile, pyridine, and di*iso*propyl ether. These results are discussed in comparison with the values previously found in benzene and in the parent alcohols and it is suggested that the donor power of the solvent has the major influence in determining the molecular complexity of the alkoxide.

EARLIER work (*J.*, 1955, 726) on the normal alkoxides of tantalum, $Ta(OR)_5$ where R = Me, Et, Pr^n, or Bu^n, showed these compounds were practically dimeric in boiling benzene whilst in the boiling parent alcohols the order of molecular complexities was: ethoxide > propoxide > butoxide > methoxide. It was suggested that the main factors likely to cause the peculiar order of complexities in the parent alcohols were (i) boiling point, (ii) dielectric constant, and (iii) "donor power" of the alcohol. In an attempt to assess the different contributions made by these factors we have determined the molecular weights of these alkoxides ebullioscopically in various solvents. Although it was not possible to choose suitable solvents in which the effects of these factors could be completely isolated from each other the results, which are presented in Table 1, show some significant features.

TABLE 1.

R in $Ta(OR)_5$	Molecular complexity in: C_6H_6 (b. p. 80°, *D* 2·28)	PhMe (b. p. 110°, *D* 2·38)	MeCN (b. p. 82°, *D* 38·8)	Pyridine (b. p. 114°, *D* 12·5)	Pr^i_2O (b. p. 68°, *D* ~3)	ROH
Me	1·98	1·83	1·50	1·01	1·75	1·20
Et	1·98	1·83	1·50	0·99	1·84	1·78
Pr^n	1·95	1·83	1·50	0·99	1·84	1·70
Bu^n	2·02	1·83	1·48	0·99	1·84	1·40

The values for the boiling point and the dielectric constant (at 20°) are recorded in parentheses for each solvent.

The general picture is that for benzene, toluene, acetonitrile, or pyridine there is no appreciable variation of molecular complexity from one alkoxide of tantalum to another, although the complexities are clearly dependent on the nature of the solvent. The pentamethoxide appears anomalous in di*iso*propyl ether in which the other alkoxides all have the same complexity. We suggest that the difference in the complexities found in benzene and toluene is caused by the effect of temperature alone because these solvents are very similar in dielectric constant and "donor power." Moreover, the decrease in complexity with increase in boiling point is in accord with the prediction that increase in temperature should promote the dissociation of the dimeric alkoxides.

The results in Table 1 suggest a value of ~40 kcal./mole as a rough estimate of the energy of dimerisation. This gives the energy of each intermolecular Ta–O bond as ~20 kcal. in the dimer. Next we consider the effect of dielectric constant bearing in mind that solvents of high dielectric constant usually have marked donor properties. However the data for acetonitrile and pyridine lead us to the opinion that dielectric constant cannot

be of major importance. Thus, when allowance is made for the effect of temperature, the complexity in acetonitrile (*D* 38·8) should be 1·35 to be comparable with the value 1·00 in boiling pyridine (*D* 12·5) and, the influence of donor power being ignored, it appears that increase in dielectric constant causes an increase in complexity. However, if the intermolecular bonding were electrostatic, *i.e.* $\overset{\delta+}{\text{Ta}}\cdots\overset{\delta-}{\text{O}}$, we should expect an increase in dielectric constant to decrease the molecular complexity by lowering the energy of dissociation. If the intermolecular bonding is essentially covalent, *i.e.*, $\overset{-}{\text{Ta}}\text{–}\overset{+}{\text{O}}$, then the formal charge separation in the covalency may neutralise the dipole $\overset{\delta+}{\text{Ta}}\text{–}\overset{\delta-}{\text{O}}\text{R}$ originally present in the monomer and thus cause a net reduction of charge separation in the dimer. In this case the effect of dielectric constant would be similar to that in the system involving electrostatic bonding. Only in a system where the formal charge separation due to covalency gave rise to a higher charge separation (of opposite sign) in the dimer would the increase in dielectric constant cause an increase in molecular complexity, *viz.*:

$$\begin{matrix}\overset{\delta_1+}{\text{Ta}}\text{–}\overset{\delta_1-}{\text{OR}} \\ + \\ \overset{\delta+}{\text{Ta}}\text{–}\overset{\delta-}{\text{OR}} \\ \text{Monomer}\end{matrix} \longrightarrow \begin{matrix}\overset{\delta_2-}{\text{Ta}}\text{–}\overset{\delta_2+}{\text{OR}} \\ | \quad | \\ \underset{\delta_2+}{\text{RO}}\text{–}\underset{\delta_2-}{\text{Ta}} \\ \text{Dimer}\end{matrix} \quad \text{where} \quad \delta_2+ > \delta_1+, \text{ and } \delta_2- > \delta_1-$$

This last possibility seems extremely unlikely and we conclude that in this comparison of pyridine with acetonitrile the effect of dielectric constant is overshadowed by differences in donor power. By donor power we mean the tendency of the solvent molecule to co-ordinate with the tantalum alkoxide by donating a lone pair of electrons to the electrophilic tantalum atom as shown in the equation:

$$[\text{Ta(OR)}_5]_2 + 2\text{S:} \rightleftharpoons 2\text{S:Ta(OR)}_5$$

According to this equation we should expect a solvent with a high donor power to promote dissociation of the dimeric tantalum alkoxide. Both acetonitrile and pyridine could be donors by virtue of their nitrogen, but the much higher basicity of the pyridine suggests that it has the higher donor power. Therefore, although pyridine has a much lower dielectric constant than acetonitrile its greater donor power is seen to be more effective in dissociating the dimeric tantalum alkoxide. The importance of donor power is confirmed by the fact that the complexity falls from benzene (*D* 2·28) to di*iso*propyl ether (*D* ~3) in spite of the opposing effect due to the lowering in boiling point. Nevertheless, the effect of the ether on the complexity is not very marked but this may well be due to stereochemical factors. Thus the donor tendency of the ether molecule may be opposed by the steric hindrance to co-ordination caused by repulsion between the alkoxide groups in the tantalum compound and the branched alkyl groups of the ether. Moreover this would explain the anomalous behaviour of tantalum methoxide in this solvent because steric hindrance should be smallest for this alkoxide.

The behaviour of the tantalum alkoxides in their parent alcohols remains to be discussed. We are inclined to the view that the fall in complexity from ethoxide to propoxide to butoxide is mainly due to the steady rise in boiling point of the solvent. The anomalous behaviour of tantalum methoxide in methyl alcohol is probably the result of several factors but the main cause is presumably that methyl alcohol has a higher donor power than the other alcohols.

It is of interest that the behaviour of thallous methoxide in boiling methyl alcohol also appears anomalous. Thus it was shown by Sidgwick and Sutton (*J.*, 1930, 1461) that in freezing benzene both thallous methoxide and ethoxide were tetrameric. However, whilst the ethoxide was also tetrameric in boiling ethyl alcohol the methoxide was monomeric in boiling methyl alcohol.

Experimental

The tantalum alkoxides were prepared and purified by the methods previously described (*loc. cit.*).

Purification of Solvents.—Toluene (" AnalaR ") was refluxed over sodium for several hours

and then distilled. Pyridine (" AnalaR ") was dried azeotropically with benzene and then fractionally distilled. Acetonitrile was purified by extraction with saturated aqueous potassium carbonate, dried by storage over repeated batches of fresh phosphoric oxide, and finally distilled. Di*iso*propyl ether was treated with ferrous sulphate solution to remove peroxides, then dried ($CaCl_2$ under nitrogen) in a dark bottle, sodium was added, and the ether fractionally distilled.

Ebullioscopy.—The construction and operation of the ebulliometer have been described (*J.*, 1955, 3977). To improve the precision of the molecular-weight determinations to *ca.* ±0·5% several " runs " were made on freshly distilled samples. In addition, a new technique of " internal calibration " was employed. Several additions of alkoxide were made to the boiling solvent and the elevations of boiling point recorded. Then several additions of a pure inert organic solute (fluorene) were made. The graph of ΔT *versus* m then took the form of two intersecting straight lines from whose slopes, and together with the molecular weight of fluorene, the apparent molecular weight of the alkoxide was calculated. In this method the result is independent of the ebullioscopic constant for the solvent or the weight of solvent. Azobenzene was also tried in place of fluorene in the " internal calibration " but was sometimes unsatisfactory owing to interaction with the tantalum alkoxide, presumably by co-ordination through nitrogen. Thus the addition of azobenzene to a benzene solution of the methoxide gave a non-linear ΔT–m, consistent with interaction of azobenzene with the methoxide (where m is the amount of solute added). However, in boiling methyl alcohol there appeared to be no interaction because two straight lines were obtained from which the correct molecular weight of the methoxide was deduced. Clearly, the donor tendency of the azobenzene was swamped by the overwhelming excess of methyl alcohol which is a donor solvent. Similar behaviour was found when azobenzene was used as an internal calibrating agent for tantalum ethoxide. Before acetonitrile, pyridine, or di*iso*propyl ether was used as solvent their effect on the tantalum alkoxides was investigated. In all cases the pure alkoxide was recovered unchanged after removal of solvent. When ethyl methyl ketone was tried with either the methoxide or the ethoxide the remaining tantalum compound had a low tantalum content. Thus it appears that a Meerwein–Ponndorf reduction occurs with partial conversion of the original tantalum alkoxide into the *sec.*-butoxide. This reaction precluded the use of ethyl methyl ketone or other ketones as ebulliometric solvents. Typical results are presented in Table 2.

TABLE 2.

Alkoxide	Range of m (g.)	Toluene (g.)	$\Delta T/m$	M Found	M Calc.
$Ta(OMe)_5$	0·024—0·227	15·19	202 •	614	336
$Ta(OEt)_5$	0·048—0·215	17·18	148	741	406
$Ta(OPr^n)_5$	0·076—0·272	15·96	130	903	476
$Ta(OBu^n)_5$	0·053—0·268	15·99	114	1033	546
		MeCN (g.)			
$Ta(OMe)_5$	0·024—0·349	14·71	0·146°	502	336
$Ta(OEt)_5$	0·092—0·549	16·23	0·108	612	406
$Ta(OPr^n)_5$	0·110—0·389	14·29	0·106	712	476
$Ta(OBu^n)_5$	0·063—0·341	14·96	0·089	810	546
		Pyridine (g.)			
$Ta(OMe)_5$	0·040—0·243	17·08	256 •	338	336
$Ta(OEt)_5$	0·052—0·336	17·05	216	401	406
$Ta(OPr^n)_5$	0·094—0·276	19·76	158	473	476
$Ta(OBu^n)_5$	0·069—0·233	18·43	147	545	546
		Pr^i_2O (g.)			
$Ta(OMe)_5$	0·042—0·435	12·84	0·514°	588	336
$Ta(OEt)_5$	0·070—0·524	12·27	0·424	747	406
$Ta(OPr^n)_5$	0·074—0·437	12·34	0·363	867	476
$Ta(OBu^n)_5$	0·067—0·629	13·92	0·279	1060	546

• ΔT = Elevation of b. p. in terms of mm. of water pressure difference in the water thermometer.

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3. *The Absorption Spectra and Stability of Complex Ions.*

By R. J. P. Williams.

The stability and absorption spectra of complex ions, particularly of transition-metal cations, are discussed with special reference to crystal-field theories. It is maintained that in its present form the theory makes unrealistic assumptions about the strength of the electrostatic field produced by different ligands. The molecular-orbital description of the interaction between ligand and cation does not suffer from the same disadvantages (van Vleck, *J. Chem. Phys.*, 1935, **3**, 807). The stability and absorption spectra of some complex ions are examined from the latter point of view.

Two explanations have been offered for the stability and absorption spectra of complex ions with special reference to the transition-metal complexes. The first depends entirely on considerations of the electrostatic potential energy of the complex in relation to that of its component ligands and cation. Essentially the theory has two parts: (1) the simple interaction of the charge of any cation and the charges or dipoles of the ligands, account being taken as far as possible of mutual polarisation (Van Arkel and de Boer, *Rec. Trav. chim.*, 1928, **47**, 593); and (2) the increase in the potential energy of electrons in degenerate states of a cation due to perturbation energy terms which must be included in the wave functions of the electrons when the latter are subjected to an electrostatic field. The second part of this description will be called the crystal-field theory (Bethe, *Ann. Physik*, 1929, **3**, 133) and is only applicable to transition-metal cations. Recently, this theory has been used in an attempt to account for features of the stability and absorption spectra of many complex ions. It is suggested below that the interpretations are unsatisfactory.

The alternative theory used in the discussion of complex ions has three different approaches. They all consider the bonding in complexes as, in part, covalent. The earliest description, that of Pauling (*J. Amer. Chem. Soc.*, 1931, **53**, 1367), lays stress on the available *empty* atomic orbitals of the cation which accept electrons from the full orbitals of the ligand. This valence-bond treatment which will be assumed to be well known, overstressed the importance of certain linear combinations of atomic orbitals (cf. Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332). The second consideration of covalent forces was developed by van Vleck (*loc. cit.*) and used the molecular-orbital method. Whereas in Pauling's treatment empty orbitals of the cation must be available, in the molecular-orbital method any d orbital of a cation together with a σ orbital of the ligand, occupied by two electrons when not bonding, gives a σd bonding and a corresponding σd^* antibonding orbital (p. 10). The electrons are fed into the most stable states one at a time and the bonding that develops will depend upon the number of electrons in these states, amongst other things. The third description of covalent forces in complexes has grown empirically from a study of the stability of complexes of the transition-metal cations in solution. In this work a close correspondence was observed between the ionisation potential of a bivalent transition-metal cation and the stability of its complexes (Irving and Williams, *J.*, 1953, 3192; Williams, *J. Phys. Chem.*, 1954, **58**, 121). The implication here is that the cation acts as an electron acceptor. If this idea is to be put into valence-bond terms, difficulties arise over the choice of the orbitals of the cation which act as the acceptors. Two theories have been given, neither of which is wholly satisfactory. An example makes this clear.

The paramagnetic complexes of bivalent nickel are octahedral. Two valence-bond descriptions of these bonds have been given, one in terms of $4s4p^3$ resonating hybrid orbitals, and the other of $4s4p^34d^2$ orbitals. The bonding is through empty orbitals of the cation only. But the stability of many nickel complexes, as compared with that of other similar cation complexes, is proportional to its ionisation potential (but see p. 12). Atomic spectroscopy has shown that the ionisation of the nickel atom leads to a univalent ion of ground state $3d^9$, so that the second electron is removed from the $3d$ shell (Menzies, *Proc. Roy. Soc.*,

1929, *A*, **122**, 134).* The ionisation potential to the state Ni^{II} is a measure of the stability in part of electrons in 3*d* atomic orbitals. These orbitals must take part in the bonding of ligands if the dependence on ionisation potential is to be explained, but they are not included in the above valence-bond descriptions. The molecular-orbital treatment of the nickel complexes, on the other hand, suggests that part of the bonding is due to $3d\sigma$ bonding orbitals (p. 10). This description leads to a similar stereochemistry for the transition-metal cations to that given by the crystal-field theory, and on these grounds it is not possible to choose between them (van Vleck, *loc. cit.*). It should be noted that there is no need to involve outer 4*d* orbitals in discussing the octahedral configuration in these complexes.

The crystal-field description of the stereochemistry of transition-metal cations has been summarised recently by Orgel (*J.*, 1952, 4756). In a cubic field which arises in many transition-metal complexes, *e.g.*, those of nickel, the five 3*d* electron states are split into a lower triplet, d_ϵ states, and an upper doublet, d_γ states. The latter point in the direction of the ligands producing the field, and the former bisect its co-ordinates. The method shows that electrostatic repulsions between the field and the *d* electrons are reduced to a minimum when the electrons fill the d_ϵ before the d_γ states. Such is the case in paramagnetic Ni^{II} complexes when the two unpaired electrons are placed in d_γ levels. This division of the electrons stabilises the complex relative to its state in the absence of splitting but in the same field. It also predicts the correct stereochemistry for a number of transition-metal cations, though the splitting of levels varies in complexity. Orgel (*loc. cit.*), in a discussion of the heats of hydration of the cations, rightly pointed out that this stabilisation should be considered when examining the stability of complexes. In order to assess the magnitude of the term he calculated from spectroscopic data the energy difference, Δ, between the state of the cation in the absence of splitting and its state in the field of the water molecules of the hydration sphere. The value, Δ, was then subtracted from the experimental heat of hydration to give the heat of hydration of the cation in the absence of cubic field splitting. These " heats of hydration " of non-degenerated cations are not related to characteristic properties of the isolated ions such as their radii or ionisation potentials. Elsewhere in the Periodic Table when cations with non-degenerate electron configurations are examined there is an empirical relation between heat of hydration and radius and ionisation potential (Williams, *loc. cit.*). This suggests that the correction applied by Orgel to the experimental heats of hydration of degenerate states is of a kind different from that considered by him. Now the difference between the excited and the ground spectroscopic states of complexes, *h*, can be shown from a molecular-orbital treatment (p. 10) to be related to the overall stability of certain bonding and anti-bonding orbitals of the two states. The difference between the states is represented in terms of the partial covalent bonding between the ligand and the cation. It will be shown, in outline, that this covalency is related to the ionisation potential of the cation so that a relation appears between *h*, and thence Δ, and ionisation potential. Orgel's corrected " heats of hydration " excluded stabilisation which belonged properly to the state of the cation in the absence of splitting by purely electrostatic fields.

Bjerrum and his collaborators (at least ten papers have been published recently; for references see Jørgensen and Bjerrum, *Acta Chem. Scand.*, 1955, **9**, 180) following Ilse and Hartmann (*Z. Naturforsch.*, 1951, **6a**, 751), who re-introduced the crystal field in discussions on complexes, also omit consideration of covalency. In fact these authors go so far as to describe donor bonds as a " peculiar " hypothesis in co-ordination chemistry. In their account, which is based entirely on electrostatic considerations, the various stabilities of degenerate ionic states in crystal fields of different symmetry have been calculated for a number of cations. In an earlier article it had been indicated that it would be possible to make such calculations but that there was already evidence to show that stereochemistry in

* It is not generally realised that the ionisation of a transition metal often induces an electronic rearrangement. In the first transition series the states of the atoms are $Cr(3d^54s^1)$, $Mn(3d^54s^2)$, $Fe(3d^64s^2)$, $Co(3d^74s^2)$, $Ni(3d^84s^2)$, $Cu(3d^{10}4s^1)$. Ionisation gives $Cr^+(3d^5)$, $Mn^+(3d^54s^1)$, $Fe^+(3d^64s^1)$, $Co^+(3d^8)$, $Ni^+(3d^9)$, $Cu^+(3d^{10})$. Further ionisation removes all the remaining 4*s* electrons. When comparing the stability of complexes with ionisation potentials it should be noted that the latter do not refer to strictly comparable states. The wave functions of the electrons ionised are mixtures of *s*, *p*, and *d* atomic wave functions, mixtures which change from atom to atom.

the transition-metal cations was in part controlled by covalency even in Pauling's supposedly "ionic" complexes (Williams, Proc. Symp. Co-ordination Chemistry, Danish Chemical Society, Copenhagen, **1954**, pp. **56**, **68**). More recent evidence strongly supports this conclusion.

The strongest evidence of the unsatisfactory nature of the crystal-field theory is its failure as an absolute method. The usual calculation of the energy states of the *d* electrons in a crystal field (Ilse and Hartmann, *loc. cit.*) leaves one parameter, Q, the strength of the field, undetermined. The parameter is evaluated from the absorption spectra of the complex. It is used as a fitting constant, every complex giving a different value of Q. If the theory were satisfactory it should be possible both to calculate a reasonable value of Q on the basis of a model for any given complex and to correlate empirically determined values of Q generally with the properties of the cations and ligands comprising the complexes. The former approach was made by Kleiner (*J. Chem. Phys.*, **1952**, **20**, **1784**), who was unable to find a suitable electrostatic model for a cubic field which gave values of Q of the correct size. He showed that one way of obtaining better values would involve covalent terms in the bonding. In the second approach, the experimental determination of Q and its correlation with properties of the ligands and cations, there have been several studies. Owen (*Proc. Roy. Soc.*, **1955**, *A*, **227**, **183**) summarised the values obtaining in a number of octahedral hydrates and observed that Q was not a simple function of ionic charge or radius of the cation. He also went on to consider covalency in the complexes. Bjerrum (*loc. cit.*) uses a slightly less obvious method of comparing spectra with the ligand field constant Q. The fitting constant in his method is the ligand polarisability, *i.e.*, anomalies in Q are always hidden in chosen values of polarisability. The frequency of the maximum in the absorption spectra of complexes of cobaltic, chromic, cupric, and nickel was found to follow the ligand order $CN^- > o$-phenanthroline $> NO_2^- >$ ethylenediamine $> NH_3 > SCN^- > H_2O > F^- > R{\cdot}CO_2^- > OH^- > Cl^- > Br^-$. By assuming unrealistic values for the polarisability of these ligands it was, of course, possible to conclude that the series came about through the influence of different fields Q. There are peculiar features about this order: unsaturated ligands give the strongest "fields," neutral molecules give stronger "fields" than anions, hydroxide even gives a weaker "field" than water. Moreover, the absorption spectra of other cations, such as ferric and cobaltous, in their complexes show maxima with frequencies in entirely different orders from the above. In order to explain the series of the frequency maxima of the ferric complexes of $CN^- > H_2O > R{\cdot}CO_2^- > Cl^- > SCN^- > o$-phenanthroline, another series of polarisabilities would be required. The different orders do find explanations on the molecular-orbital theory.

The Molecular-orbital Theory.—According to van Vleck (*loc. cit.*) there are bonding and anti-bonding orbitals between combinations of ligand σ orbitals (which will be linear combinations themselves of atomic *s* and *p* orbitals) and d_γ orbitals of the cation which can be written as:

Bonding $$\sigma d_\gamma = (1 - \alpha^2)^{\frac{1}{2}} d_\gamma + \alpha f(\sigma) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Anti-bonding $$\sigma d_\gamma^* = \alpha d_\gamma - (1 - \alpha^2)^{\frac{1}{2}} f(\sigma) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

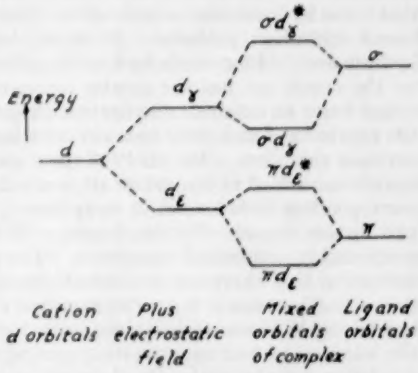
where α is an admixture coefficient and f represents a function of the σ orbitals of the ligands and is also dependent upon the symmetry of their arrangement about the cation. If the d_γ orbitals are not involved in covalent bonding, then α is unity. Apart from these orbitals there will be π orbitals not considered by van Vleck but described by Kimball (*J. Chem. Phys.*, **1940**, **8**, **188**) for the case where the ligand acts as an acceptor, and by Griffiths and Owen (*Proc. Roy. Soc.*, **1954**, *A*, **226**, **96**) for the case where the cation acts as an acceptor. They are:

Bonding $$\pi d_\varepsilon = \beta d_\varepsilon + (1 - \beta^2)^{\frac{1}{2}} f'(\pi) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Anti-bonding $$\pi d_\varepsilon^* = (1 - \beta^2)^{\frac{1}{2}} d_\varepsilon - \beta f'(\pi) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where β is an admixture coefficient and f' is a function of the π orbitals of the ligand and their symmetry with regard to the central metal cation. If π bonds are not involved in the complex then β is unity.*

If there are no σd_γ* anti-bonding electrons then expression (1) is of the same form as in valence-bond treatments, and likewise if there are no πd_ε* anti-bonding electrons then the set of πd_ε bonding orbitals are the same as those described by Pauling as double bonds in carbonyls and cyanides (" Nature of the Chemical Bond," Cornell Univ. Press, New York, 1939, p. 250). It should be observed that the d_γ and d_ε orbitals in equations (1)—(4) are the perturbed wave functions used in crystal-field calculations. The effect of covalency upon the energy of these states is shown in the accompanying Figure, due to Owen (*loc. cit.*). No quantitative applications of this type of diagram can be made as yet but several qualitative observations are of interest.



Schematic representation of the formation of mixed orbitals of a complex ion from the component orbitals of the cation and the ligand. (Particular attention is directed to the footnote on this page with regard to this diagram.)

It is self-evident that the bonding orbitals in expressions (1) and (3) are of greater potential energy than the anti-bonding orbitals. As electrons are supplied to the molecular orbitals, those that are bonding are occupied first. On filling of the bonding orbitals, electrons are added to the anti-bonding orbitals until the full complement of electrons of the cation and ligand is reached. Whereas the filling of bonding orbitals stabilises the complex relative to its components in the absence of covalency, yet filling anti-bonding orbitals destabilises it (see Figure). If the anti-bonding orbitals contain as many electrons as the bonding orbitals, then the total potential energy of the electrons is highest when α and β are close to unity; there is no covalency involving *d* electrons. The coefficients α and β are evaluated, of course, so that the total potential energy is a maximum in this and other cases where the anti-bonding orbitals are not filled. It is obvious that the admixture coefficients decrease as the number of anti-bonding electrons decreases, and maximum covalency is reached when there are no anti-bonding electrons. The situation is extremely complicated in these complexes and exact expressions have not yet been derived but the overall picture is comparable with the extent of covalent bonding in He_2 and He_2^+. In the latter ion, covalency stabilises the bond, there is but one anti-bonding electron, but the neutral molecule is not stable (cf. Coulson, " Valence," Oxford, 1952, p. 94). The covalency decreases with the number of anti-bonding electrons. A comparable case is that of the bonding in the zinc complexes compared with that in the complexes of transition-metal cations immediately preceding zinc. In zinc the $3d\sigma$* anti-bonding orbitals will contain as many electrons as the corresponding bonding orbitals, with a result that α is close to unity. In the transition cation complexes α will be less than unity, as there are fewer anti-bonding than bonding electrons. Relatively to their ionisation potentials even, the zinc complexes

* This representation of the molecular orbitals formed from *d* cation atomic orbitals and other atomic orbitals of the ligand is a gross over-simplification. Linear combinations of *s* and *p* cation atomic orbitals with the former group can also be written and will add to the stability of the complex. The purpose of the present argument is to indicate the part played by the *d* orbitals, and for this reason more correct but more complicated expressions have been omitted. The qualitative conclusions drawn are not likely to be affected by the simplification.

are less stable than those of the transition-metal cations, illustrating the better bonding potentialities of *d* orbitals than of *s* and *p* orbitals.

The principal additional factor which determines the size of the covalency coefficients is the relative electron affinity of the atomic orbitals which form the molecular orbitals; the more equal these two affinities, the more covalent the bond. Now, in general, σ orbitals of the ligand have a greater electron affinity than d_γ orbitals of the cation. It is not surprising, then, that, as the ionisation potential of the cation increases and that of the ligand decreases, the complexes become more covalent. These relations are confirmed, not only by a study of the stability of complex ions, but also by an analysis of their paramagnetic absorption spectra. Owen (*loc. cit.*) showed that the values of α are smaller in tervalent than in bivalent hydrates. Comparison of the values of α in cupric and nickel hydrates with van Wieringen's data (*Discuss. Faraday Soc.*, 1955, **19**, in the press) shows that these hydrates are more covalent than that of manganous. The latter cation has the lowest ionisation potential. It should be noted that the values, $\alpha = 0{\cdot}83$, for nickel hydrate and 0·84 for cupric hydrate invalidate the comparison of α with ionisation potential, for the cupric ion has the greater ionisation potential. As Owen pointed out, however, nickel forms an octahedral hydrate with six equal bonds of 3% covalent character, whereas the cupric ion forms only four covalent bonds involving *d* orbitals each of which has 4% covalent character. The study of the stability of the cupric complexes shows the first four ligands are added in equivalent steps which involve a larger free-energy change than in the corresponding nickel series of complexes. The position is reversed during the addition of two further ligands (Davies, Singer, and Staveley, *J.*, 1954, 2304), and nickel forms the more stable octahedral complexes. The paramagnetic resonance measurements agree in indicating that there are individually more covalent bonds in cupric complexes but that the overall covalency is greater in nickel complexes. Despite the general applicability of the Irving–Williams stability sequence to the formation constants of complexes involving the addition of four co-ordinating groups, it is not applicable to six-co-ordination, and in the latter complexes the parallel with ionisation potential is broken. The reasons for the failure of the correlation are apparent from equations (1) and (2). The cupric complexes are reduced in stability by the additional electron in the anti-bonding orbitals—a reduction which is not compensated by the greater stability of the bonding orbitals and has little influence until the addition of the fifth ligand because of the stereochemistry of the d_γ orbitals. The ionisation potential is not a proper measure of the overall stability of a complex, for the latter includes two unrelated energy terms, the splitting of the *d* levels by an electrostatic field (cf. Orgel, *loc. cit.*) and the directional character of $d_\gamma\sigma$ and $d_\gamma\sigma^*$ orbitals which increases or restricts covalency. Usually, however, changes in ionisation potential have sufficiently large influence to mask other factors.

Measurements by van Wieringen (*loc. cit.*) have shown also that covalency involving *d* orbitals increases along the series of manganous salts, oxide, sulphide, selenide, telluride, which is the order of ease of ionisation of the anions. The paramagnetic absorption method has also shown that ammines are more covalent, *i.e.*, have smaller α, than hydrates (Owen, *loc. cit.*).

So far, the discussion has centred about the size of the α coefficients. Unlike the values of α, those of β can be small through electron-donor as well as -acceptor properties of the ligand. Unsaturated ligands accept electrons from the d_ε orbitals (see, *e.g.*, the work of Calvin and Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2003). Now, in such complexes the molecular orbitals spread over the entire complex, and stability should increase with the number of ligands in a complex. Data in the literature (cf. Irving and Williams, *loc. cit.*) show that, in accordance with this idea, the differences between the step stability constants are smaller for chelating aromatic ligands than for similar aliphatic compounds; *e.g.*, compare the values for complexes of glycine with those of 8-hydroxyquinoline, or ethylenediamine complexes with those of phenanthroline. Other aspects of this type of πd_ε bonding have been considered by Craig, Maccoll, Nyholm, Orgel, and Sutton (*loc. cit.*). It may well have a decisive influence on the preferred stereochemistry of complexes even outside a transition series. For example, the aliphatic ammines of zinc are generally tetrahedral, but the aromatic ammines show no tendency to remain four co-ordinated and the cation has octahedral complexes in these cases.

The ligand may also act as a π electron donor. As the ionisation potentials of neutral ligands, such as water, are relatively higher than those of anions, it is to be expected that π-electron donation will only be strong in anionic complexes. The paramagnetic absorption spectra of a number of complexes indicate that this type of covalency is weak even in tervalent hydrates but that it is strong in many halide complexes. The following interpretation of the absorption spectra of some complex ions would strongly favour these suggestions.

The Absorption Spectra of Some Complex Ions.—The theory that will be given here has already been outlined in a discussion of the absorption spectra of ferric complexes (Williams, *J.*, 1955, 137). It considers the difference in covalency between the ground and the excited spectroscopic states brought about by the changed occupation of the orbitals given in equations (1)—(4). All the transitions to be examined arise from the splitting of the *d* states. The absorption bands are often, but not always, weak, therefore, because the transitions are formally forbidden. It is useful to divide the transitions into two kinds, those involving a change of multiplicity and those involving no such change. The former are the more strongly forbidden by selection rules. The latter will be discussed first by taking a typical example, the cupric complexes.

In cupric hydrate the 3*d* electrons of the cupric ion and the electrons of the σ and π orbitals of the water molecules are divided amongst the molecular orbitals shown in the figure. The πd_ϵ and πd_ϵ^* orbitals, which are lowest, are fully occupied and there are then three electrons remaining for each pair of σd_γ and σd_γ^* orbitals. The latter are of the greater energy and are only half filled. In the ground state of the cupric ion, then, β will will be close to unity, πd_ϵ^* will be filled, but α will be considerably less than unity (p. 11). On excitation by the absorption of light, an electron of the anti-bonding πd_ϵ^* orbitals is excited into one of the σd_γ^* orbitals. It follows from the discussion on p. 11 that the value of α must rise to nearly unity, for the anti-bonding orbital σd_γ^* is now full. There is a loss of covalency and a concomitant change in polarity in the complex on excitation. The transition which is related to a forbidden atomic transition will become, in terms of the mixed orbitals, less strongly forbidden because of its association with a polarity change. In this way an apparent breakdown of selection rules is observed. The fact that β will have become less than unity in the excited state, the πd_ϵ^* orbitals not being fully occupied, has so far been ignored. The concomitant change in πd_ϵ covalency will produce a polarity change in the opposite direction from that given by the change in σd_γ covalency. However, the change in β is believed to be small in cations of the first transition series when they are bound to neutral ligands, and it is probably the case that the change in α represents the major change in polarity. Now the probability of a given transition is related to the change in polarity which it brings about and to the area under the maxima of the absorption spectrum curve with which it has been identified. In a series of similar complexes the areas under absorption peaks can be roughly obtained from the maximum extinction coefficients. This extinction coefficient should be found to increase with increasing covalency in the ground state in a series of cupric complexes : it should increase with the σ donor properties of the ligand. Experiment strongly supports this conclusion. For example, changing the ligand attached to the cupric ion from water to ammonia, or along the series of substituted amines, ammonia, ethylenediamine, diethylenetriamine, triethylenetetramine, tetraethylenepentamine (Irving and Griffiths, *J.*, 1954, 213) or from chloride to bromide, increases the intensity of the cupric absorption band at long wavelength, a *d*–*d* transition, which follows the donor character of the ligands. Very similar observations have been made on the absorption spectra of complexes of nickel, cobaltic, and chromic. In each case the absorption maximum increases in intensity from water to ammonia to ethylenediamine complexes. In titanous and vanadous complexes the intensity of absorption increases along the series water, alcohol, ether, or along the series methanol, ethanol (Hartmann and Schläfer, *Z. phys. Chem.*, 1951, **197**, 116; *Z. Naturforsch.*, 1951, **6a**, 754, 760). If a series of cations are compared in their complexes with one ligand, then according to the above discussion the intensity of the absorption should increase with the ionisation potential of the cation. In the bivalent series of hydrates and ammines $Cu^{II} > Ni^{II} > Co^{II} > Fe^{II}$ this parallel is found. Elsewhere (Williams, *loc. cit.*) the change in intensity in other series of complexes follows the ionisation potential of the cation rather than any

function of the radius and charge which might have indicated that polarisation by electrostatic forces was important.

The positions of the absorption maxima in many complexes can also be interpreted with the aid of equations (1)—(4) and the Figure. A transition from a πd_ε^* orbital to σd_γ^* will involve a greater energy change the greater the covalency, σd_γ bonds, in the complex. This covalency gives an increase in the splitting of the d_γ and d_ε electronic states which must be added to the effects produced by the electrostatic field of the ligands alone. As the intensity of the electrostatic field due to a given ligand is unlikely to parallel its ability to form co-ordinate covalent bonds, the total splitting cannot be calculated at all readily. This complication, which is absent from considerations of the intensities, makes all discussion more difficult. In those complexes where β is expected to be close to unity in both the ground and the excited spectroscopic states, increasing covalency in a complex should move a given transition to shorter wavelengths as the splitting between σd_γ^* and πd_ε^* is increased. This is observed in the movement of the weak bands of chromic, cobaltic, cupric, nickelous, and cobaltous on replacement of the water molecules of the hydrate by ammonia or, to a greater extent, by ethylenediamine. Moreover, the shift in the individual cation complexes follows the change in covalency in the complex. During the addition of the first four ligands, the largest shift occurs in the order $Cu^{II} > Ni^{II} > Co^{II}$; as pointed out earlier, this is the order of the ionisation potentials of these cations. Now, on p. 12, it was shown that the nickel complexes exceed the cupric complexes in covalency on the addition of the last two ligands, making a hexaco-ordinate complex, despite the order of the ionisation potentials. This is also reflected in the absorption spectra, the shift from the hydrate to the hexammine being greatest in the order $Ni^{II} > Cu^{II} > Co^{II}$. Such observations as these can only be explained on crystal-field theory by assuming a different relative polarisability for water and ammonia in each cation complex, and sometimes different relative polarisabilities for the different steps of the complex formation (cf. Bjerrum *et al.*, *loc. cit.*, who list the relevant absorption spectra).

The omission of effects due to changes in β in the discussion of the position of the absorption spectra of complexes is probably only justifiable where the ligands are saturated uncharged compounds such as ammonia and water (p. 13). The effect of mixing d_ε orbitals of the cation with ligand π orbitals can produce two additional effects. If the ligand is unsaturated, then the mixing with empty orbitals lowers the d_ε states of the cation. But there are now no anti-bonding electrons so that it is these highly stabilised πd_ε bonding electrons which are excited to the σd_γ^* anti-bonding states. The absorption maxima are shifted to short wavelengths by unsaturated ligands. In fact, the absorption bands of the cations, nickel, cobaltous, chromic, cobaltic, and cupric move to shortest wavelengths with cyanide and phenanthroline. However, the stabilisation of the d_ε electrons is observed even in the pyridine complexes of cupric. Despite the fact that pyridine is a much weaker base than ammonia, the bands in the cupric complexes of the former are at the shorter wavelength (Bjerrum and Nielsen, *Acta Chem. Scand.*, 1948, **2**, 297). On the other hand, if a ligand acts as a π electron donor, then the d_ε electrons of the cation are accommodated in elevated πd_ε^* orbitals, with the result that the excitation to σd_γ orbitals is energetically easier—the absorption band moves to longer wavelengths. It has already been mentioned that paramagnetic absorption spectra indicate that anions such as chloride seem able to act as better π electron donors than neutral molecules. Part of this effect may arise from the fact that the neutral molecules so far used as ligands are derived from first-period elements, oxygen and nitrogen, whereas the anions examined include chloride and bromide. In general, the directional characteristics of orbitals of higher principal quantum number are better than those of earlier shells. Be this as it may, the position of the absorption bands of anions is generally at much longer wavelengths, in agreement with predictions that can be made from the paramagnetic measurements. The order of the position of the absorption band maxima for different ligands with one cation, *i.e.*, unsaturated ligands, saturated neutral molecules, anions, is now seen to be a result of the variety of bonding that can arise in a complex and cannot be directly related to one of the factors in the bonding, namely, the electrostatic field.

When the ground state of the complex is non-degenerate, as in ferric complexes,

transitions require a change of spin multiplicity which is strongly forbidden by the selection rules. Absorption in the simple hydrates of such ions is extremely weak. In the ferric complexes, for example, the ground state is ^6S and the first excited state ^4G. An analysis of the very weak absorption bands which result from transitions between these states has been made by Schläfer [*Z. phys. Chem.* (*Frankfurt*), 1955, **4**, 116]. When the ferric ion is bound to any ligand that can act as a π electron donor, however, the intensity of the absorption rises, sometimes even reaching values comparable with those of fully allowed transitions (Williams, *loc. cit.*). Here it is the excited state which is the better acceptor, for the excitation of an electron from the ground state leaves an empty orbital, probably a πd_ϵ orbital. Further, the absorption bands in the ferric complexes move to longer wavelengths the better the donor properties of the ligand. This shift is in the opposite direction from that found in the complexes described earlier, *e.g.*, of Cu^{II}, where the transitions took the cation to a bonding state of lower potential covalency than the ground state. It appears difficult to explain these different observations in terms of the crystal-field theory.

Finally, it is clear that if the covalency described becomes sufficiently strong, the antibonding orbitals may be destabilised to such an extent that they are of higher energy than another state of lower multiplicity. In such a case a change of magnetic moment is observed in the ground state (van Vleck, *loc. cit.*).

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4. *Thermochromism of Compounds containing the Thiocarbonyl and Disulphide Functions.*

By J. C. D. BRAND and J. R. DAVIDSON.

The spectra in solution of some thiocarbonyl compounds and disulphides have been measured in the temperature range 20—115°. The visual thermochromism of the thiocarbonyl compounds is associated with the first ($N \longrightarrow A$) electronic absorption band and is due to a redistribution of intensity with temperature, the integrated intensity remaining constant; at high temperature the band broadens and moves slightly (100—150 cm.$^{-1}$) to lower frequencies. The broadening is attributable to the change with temperature of the relative population of the lower vibrational levels of the ground state; the frequency shift is a new effect, explained by a diminution of solvent–solute interaction with rising temperature.

Di-1-thionaphthoyl disulphide obeys Beer's law at 100°, but a slow, irreversible decomposition occurs at this temperature. With di(benzothiazol-2-yl) disulphide, the thermochromism (to 100°) is due to thermal broadening of the spectrum and not to reversible dissociation into benzothiazol-2-ylthio-radicals.

THIOCARBONYL compounds and aryl disulphides are weakly thermochromic; the thermochromism is visually not striking, but the colour of a melt or solution deepens on heating and the normal colour returns on cooling. This study is concerned with the nature of the spectral changes, and the spectra of representative compounds have been measured at normal and high temperatures. The results are probably of wider application, for most coloured substances change their colour on warming and the underlying spectral differences must also arise when absorption is entirely in the ultraviolet region.

Thiocarbonyl Compounds.—Five compounds of this class were examined (Table 1). Among them the visual thermochromism of methyl 1-dithionaphthoate (I) and diphenyl trithiocarbonate (V) has been described by Schönberg, Nickel, and Cernik (*Ber.*, 1932, **65**, 293), and 1-naphthyl phenyl thioketone (II) in solution deepens in colour from blue to blue-green on warming; the thioncarbonates (III) and (IV) do not absorb in the visible region. With all five compounds the spectral changes on heating were the same, but for reasons mentioned later the most satisfactory results were obtained with methyl 1-dithionaphthoate and 1-naphthyl phenyl thioketone.

TABLE 1. *N ⟶ A Transitions of thiocarbonyl compounds (solvents are shown in parentheses).*

	Temp.	$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$ (l. mole^{-1} cm.$^{-1}$)	$(\Delta\varepsilon)_{max.}$	Oscillator strength ($10^4 f$)
1-$C_{10}H_7$·CS·SMe (I)	20°	20,450	115	—	14·1
	60	20,420	113	8	14·2
(Ethyl Oxalate)	101	20,400	112	12	14·3
	115	20,380	111	14	14·4
1-$C_{10}H_7$·CS·Ph (II)	21	16,200	155	—	19·8
(Decalin)	81	16,100	151	14	19·8
$(PhO)_2CS$ (III)	18	30,550	45	—	2·0
(96%-Ethanol)	70	30,500	46	3	—
p-MeO·C_6H_4·O)$_2$CS (IV) ...	17	30,100	75	—	2·8
(Decalin)	81	30,100	73	5	—
$(PhS)_2CS$ (V)	19	21,750	32	—	1·0
(Decalin)	101	21,650	35	7	—

The first absorption band of the dithionaphthoate is reproduced in Fig. 1. The curves of $\Delta\varepsilon$ [$\varepsilon(20°) - \varepsilon(115°)$, etc.] are asymmetrical, being mainly positive on the red side of the absorption maximum and mainly negative on the blue; this is equivalent to a small

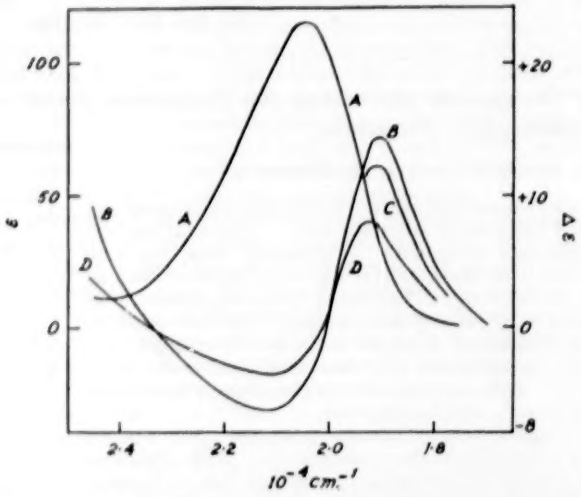

FIG. 1. *Methyl 1-dithionaphthoate in ethyl oxalate.*

A, ε (20°);
B, ε (115°) − ε (20°);
C, ε (101°) − ε (20°);
D, ε (60°) − (20°).

net transfer of intensity to the red, corresponding to the deepening of colour observed visually. The integrated intensity apparently rises slightly with temperature (Table 1), but the increment can be attributed to the proximity of a much stronger ultraviolet band (cf. Fig. 3); the broadening of the second band in the hot solution contributes some intensity to the area under the envelope of the first band. With 1-naphthyl phenyl thioketone (Fig. 2) the resolution of the first and second absorption bands is sharper and the integrated intensity of the first band is independent of temperature.

Constancy of $\int \varepsilon d\nu$ means that the number of electrons, and hence the number of molecules, excited in absorption does not vary with temperature. In this case it is almost certain that the spectral changes are not to be attributed to excitation from two (or more) discrete, lower states of unequal energy. Near-lying states of this kind might result from different conformations of the molecule (with 1-naphthyl phenyl thioketone, for example, it is most improbable that the naphthyl, phenyl, and thiocarbonyl chromophores are coplanar at equilibrium, and different rotational conformations with slightly different energies and electronic spectra are conceivable) or, possibly, from a very low-lying excited electronic state. Such an explanation is difficult to rule out, because it is impossible to

know in advance what range of temperature will be required to disclose a real change in $\int \varepsilon d\nu$, but there seems to be no evidence to support it; constancy of $\int \varepsilon d\nu$ will therefore be accepted as genuine. Granted this, the spectral changes must be attributed to the change with temperature of the population of the ground-state vibrational levels, or to a relaxation of solvent–solute interaction, or both.

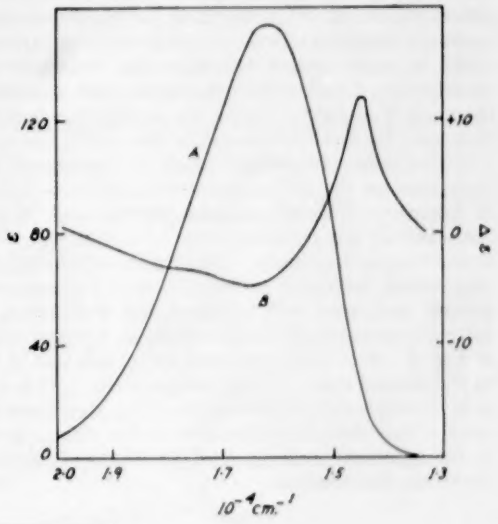

FIG. 2. *1-Naphthyl phenyl thioketone in decalin.*

A, ε (21°);
B, ε (81°) − ε (21°).

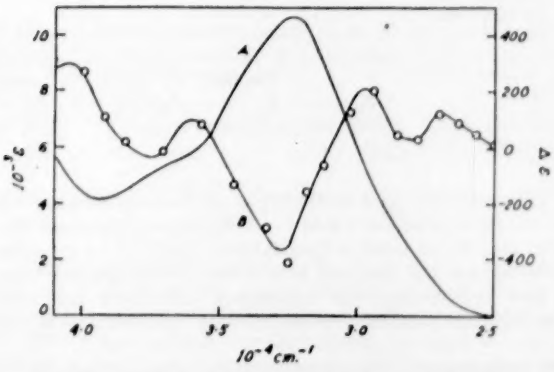

FIG. 3. *Methyl 1-dithionaphthoate in ethanol* (2500—4000 Å).

A, ε (19°);
B, ε (71°) − ε (19°).

As a consequence of the Franck–Condon principle a change in the distribution of molecules over the vibrational levels of the gound state leads to a broadening of the absorption band with rise of temperature (Grubb and Kistiakowsky, *J. Amer. Chem. Soc.*, 1950, **72**, 419). This effect, which we will term *thermal broadening*, has been observed with continuous vapour-phase spectra (Gibson, Rice, and Bayliss, *Phys. Rev.*, 1933, **44**, 193; Almasy and Laemmel, *Helv. Chim. Acta*, 1950, **33**, 2092) and is a property of the isolated molecule: the characteristic $\Delta\varepsilon$ curve associated with it has a maximum below each of the extremities of the absorption band, and a central minimum. Curves of this type were obtained in the ultraviolet spectrum of methyl 1-dithionaphthoate (Fig. 3) wherein each band, including the partly submerged bands that appear as an inflection of the spectral envelope, corresponds to a minimum in $\Delta\varepsilon$. (Where two bands are fused, as on each wing of the central 32,500 cm.$^{-1}$ peak, the maxima in the $\Delta\varepsilon$ curve are superimposed.) The first absorption band of the ester, however, does not conform to this pattern; compared with the

more or less symmetrical $\Delta\epsilon$ curve in Fig. 3, the highly asymmetrical curves in Fig. 1 suggest that, in addition to thermal broadening, there has been a movement of the whole absorption band towards the red in the hot solution. This second effect we term the *thermal shift*. As the thermal shift is important with the first absorption band only, it is unlikely that the correct explanation will be in terms of the isolated molecule: a more promising correlation is with the well-known frequency shifts observed at room temperature between different solvents. The width of the band is normal and we will assume that there is no major difference in size (or shape) of the molecule after excitation, but because the band is weak it must be inferred that the electronic distribution differs considerably, and consequently that the solvation shell, after excitation, must undergo reorganisation before the excited molecules attain the equilibrium excited state. The energies of the ground state and the equilibrium excited state will rise with temperature, as the (free) energy of solvation falls. In greater detail, the increment in energy will be larger for the ground state, because the electronic transition ($N \longrightarrow A$) is presumably associated with a decrease of (permanent) dipole moment (Bayliss and McRae, *J. Phys. Chem.*, 1954, **54**, 1002); consequently the pure electronic transition will move slightly towards the red in solution as the temperature rises. The experimental $\nu_{max.}$, however, refers to a " vertical " excited state which, because it is destabilised by the unfavourable conformation of the surrounding solvent molecules, will approach the equilibrium excited state as interaction with the solvent is increasingly broken down by thermal motion. These movements are illustrated in Fig. 4; their sum represents an overall loss of height of the " vertical " state, relative to the ground state, at high temperatures. It is shown in the Appendix that the thermal shift corresponds to a movement of the peak frequency towards the red by 100—150 cm.$^{-1}$; most of the shift is attributable to the change in energy of the vertical state, and hence to the peculiarly unfavourable conditions of solvation resulting from the major change in electronic distribution.

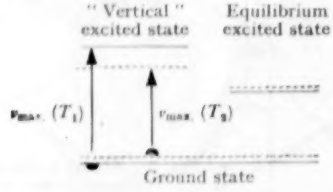

FIG. 4.

T_1 ———, T_2 ------- $(T_2 > T_1)$

The results for diphenyl thioncarbonate (III), di-*p*-methoxyphenyl thioncarbonate (IV), and diphenyl trithiocarbonate (V) are summarised in Table 1. With these compounds the influence of temperature on the first absorption band is qualitatively the same as recorded for the thionaphthoate and the thioketone but thermal broadening of the second band tends to obscure the details. For this reason the integrated intensities are only approximate, and a comparison of integrated intensities at different temperatures is not attempted.

Disulphides.—It has frequently been asserted that the thermochromism of disulphides is associated with a *reversible* dissociation equilibrium, the development of colour being assigned to the absorption of the arylthio-radicals (Schönberg *et al.*, *Ber.*, 1932, **65**, 1864; 1935, **68**, 163; *Naturwiss.*, 1933, **21**, 561; *J.*, 1949, 889; Mustafa and Kamal, *Science*, 1953, **118**, 411).* There is evidence, however, that the temperature required for thermal fission is much higher than that needed to observe the thermochromism of disulphides (Bloomfield, *J.*, 1947, 1547; Kharasch, Nudenberg, and Meltzer, *J. Org. Chem.*, 1953, **18**, 1233), and three representative compounds were examined in the present study to determine whether there is any real connection between the phenomena.

Definitive results were obtained with di(benzothiazol-2-yl) disulphide. This compound is thermochromic in solution (Koch, *J.*, 1949, 401) and the spectrum was remeasured in

* The reversibility of the dissociation follows from the putative correlation with the colour change; insofar as the original colour returns on cooling, the arylthio-radicals cannot disappear except by recombination.

decalin (18° and 80°: Fig. 5) and anisole (18° and 100°). The $\Delta\varepsilon$ curve is accounted for entirely by thermal broadening; of the four minima (A—D), B corresponds to the principal absorption maximum at 36,700 cm.$^{-1}$ and A, C, and D to the partially submerged bands at approximately 41,000, 35,000, and 33,500 cm.$^{-1}$ respectively. The main increment of intensity is at 32,000 cm.$^{-1}$ but a long tail runs into the visible region and is sufficient, in moderately concentrated solutions, to account for the visual thermochromism (in anisole, at 100°, $\Delta\varepsilon = +40$ at 4000 Å). As Beer's law is obeyed in the near ultraviolet region at 100°, it is concluded that the thermochromism, as ordinarily understood, is wholly a property of the undissociated molecule. The results do not prove that no fission occurs at 100° (except on the negative evidence that nothing in the spectrum is attributable to absorption

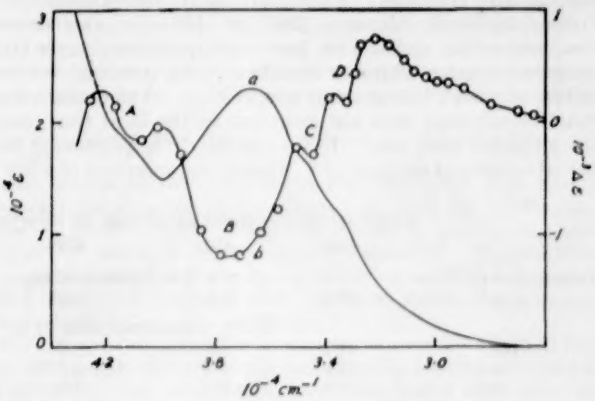

FIG. 5. *Di(benzothiazol-2-yl) disulphide in decalin.*
a, ε (19°);
b, ε (80°) − ε (19°).

by benzothiazol-2-ylthio-radicals) and, in fact, susceptibility measurements indicate a small degree of dissociation (3%) at this temperature (Cutforth and Selwood, *J. Amer. Chem. Soc.*, 1948, **70**, 278).

Di(benzothiazol-2-yl) disulphide in anisole.

λ (Å)	3800	3750	3700	3650
Concn. (10^{-5} M)		ε, 100°		
2·80	116	162	221	298
0·56	116	161	218	298

Di-1-thionaphthoyl disulphide has been investigated by Schönberg, Rupp, and Gumlich (*Ber.*, 1933, **66**, 1932) who reported failure of Beer's law at 100° and tacitly assigned a peak at 5200 Å to the 1-thionaphthoylthio-radical. Apart from the matter of the assignment (the 5200 Å band almost certainly marks the usual $N \longrightarrow A$ transition of the undissociated molecule), the failure of Beer's law was not confirmed in the present experiments. Results are given below for two wavelengths, one near the peak of the first band and the other on the shoulder of the second band, where, according to Schönberg, deviations from Beer's law are especially large. At 100°, however, the solutions were unstable and the optical density

ε for di-1-*thionaphthoyl disulphide in anisole* (*temp.* 100°).

λ (Å)	5250		4250	
Concn. (10^{-5} M)	This paper	Schönberg *et al.**	This paper	Schönberg *et al.**
5	—	150	—	55
4·64	257	—	363	—
1	—	185	—	140
0·93	254	—	372	—
0·2	—	255	—	—

* Similar behaviour was reported for diphenyl disulphide (*idem*, *loc. cit.*): this result has also been shown to be erroneous (Lecher, *Science*, 1954, **120**, 220).

slowly decreased; on cooling to room temperature some solutions (those in tetrabromoethane) were visibly turbid. It is clear therefore that irreversible fission occurs in the hot solution, probably analogous to the decomposition of benzoyl peroxide:

$$C_{10}H_7{\cdot}CS{\cdot}S{-}S{\cdot}CS{\cdot}C_{10}H_7 = 2C_{10}H_7{\cdot}CS{\cdot}S{\cdot}$$
$$\text{Products} \longleftarrow C_{10}H_7{\cdot}CS{\cdot}S{\cdot} = CS_2 + C_{10}H_7{\cdot} \longrightarrow \text{Products}$$

Di(tetramethylthiuram) disulphide, though not an aryl disulphide, was studied because it is a vulcanisation accelerator and is thermochromic; once again, the thermochromism has been correlated with dissociation (Koch, *loc. cit.*). In support of the dissociation hypothesis it has been claimed that solutions (in ethylene dibromide) do not obey Beer's law at 20° (Bergem, "Contributions to the Theory of Vulcanisation," A/S Askim Gummivarefabrik, Norway, 1948, pp. 136—7). Our measurements do not agree with this, and within rather wide limits of experimental error (the optical density of a freshly prepared solution increases considerably on standing) we were unable to detect significant failure of Beer's law at room temperature. The explanation of Bergem's results may be that the solutions were not examined at the same time, and it is noteworthy that his ε's are all higher than ours. In view of the decomposition at room temperature (probably by initial scission of the central S–S bond) the spectrum of a hot solution was not examined.

Di(tetramethylthiuram) disulphide in ethylene dibromide.

λ (Å) / Concn. (10^{-5} M)	4050	4200	4340	4500	4630
		ε (20°) of a fresh solution			
103	11·2	4·38	1·95	0·76	0·37
		ε (20°) of a solution after 24 hr.*			
103	12·4	5·5	2·7	1·1	0·53
50·5	12·6	5·4	2·6	1·1	0·51
10·2	12·2	5·2	2·5	1·1	0·54
		ε (20°) according to Bergem			
50	—	—	4·46	—	1·80
1·5	—	—	14·00	—	4·00

* Validity of Beer's law in the aged solution indicates that the decomposition is of the first order.

Assignments.—The recorded frequencies, intensities, and spectral assignments are summarised in Table 2. In general the assignments are straightforward, except for the

TABLE 2.

Probable assignt.*	1-$C_{10}H_7{\cdot}CS{\cdot}SMe$		1-$C_{10}H_7{\cdot}CS{\cdot}Ph$	$C_{10}H_7{\cdot}CS{\cdot}S{\cdot}S{\cdot}CS{\cdot}C_{10}H_7$	
	n-Hexane	95% Ethanol	Decalin	*cyclo*Hexane	Anisole
$N \longrightarrow A$	20,170 (2·048)	20,520 (2·048)	16,150 (2·190)	—	19,230 (2·43)
$N \longrightarrow L_b$	*ca.* 29,400 (*s*)	~28,600 (*s*)	26,700 (3·49)	28,500 (3·96) *sh*	—
$N \longrightarrow L_a$	32,700 (4·03)	32,500 (4·03)	31,500 (4·19)	33,800 (4·21)	—
$N \longrightarrow B$	37,000 (3·74) *sh*	~37,000 (*s*)	39,200 (3·93) *sh*	—	—
$N \longrightarrow B_b$	—	45,500 (4·76)	45,400 (4·76) ‡	45,500 (4·97)	—

Probable assignt.*	$(PhO_2)CS$	$(p\text{-}MeO{\cdot}C_6H_4O)_2CS$		$(PhS)_2CS$	
	95% Ethanol	Decalin	95% Ethanol	Decalin	95% Ethanol
$N \longrightarrow A$	30,450 (1·65)	30,100 (1·88)	30,770 (1·94)	21,800 (1·50)	21,980 (1·50)
	—	—	—	32,200 (4·01) †	32,500 (4·03) †
	—	—	—	35,500 (4·08) †	36,000 (3·96 †
$N \longrightarrow L_b$	~35,700 (*s*)	35,100 (3·57) *s* 36,000 (3·69) 36,900 (3·69)	35,200 (3·57) *s* 36,360 (3·69) *sh*	—	—
$N \longrightarrow B$	42,500 (3·82) *sh*	—	40,000 (*s*)	39,700 (3·84)	40,000 (*s*)
$N \longrightarrow L_a$	>46,000	—	44,400 (4·33)	—	—

sh = shoulder; *s* = submerged maximum.

Frequencies ($\nu_{max.}$) are in $cm.^{-1}$, usually to three significant figures: values of log $\varepsilon_{max.}$ are given in parentheses.

* L_a, L_b, and B_b are excited states of the (conjugated) aromatic chromophores (Platt, *J. Chem. Phys.*, 1949, **17**, 484).

† Assignment uncertain. ‡ Solution in *cyclo*hexane.

second and third transitions of diphenyl trithiocarbonate where the interpretation is uncertain. The spectra of methyl 1-dithionaphthoate (Fig. 3) and diphenyl trithiocarbonate were measured at high temperature but, with the exception of the $N \longrightarrow A$ transitions, the principal aspect was of thermal broadening.

Experimental

Microanalyses by Mr. J. M. L. Cameron and Miss M. Christie.

Materials.—*Di*-p-*methoxyphenyl thioncarbonate*, obtained by condensation of thiocarbonyl chloride with quinol monomethyl ether in aqueous sodium hydroxide, had m. p. 164·5° (Found: C, 62·1; H, 4·8; S, 11·1. $C_{15}H_{14}O_4S$ requires C, 62·1; H, 4·9; S, 11·1%). The remaining compounds were purified commercial samples or were prepared by standard methods: methyl 1-dithionaphthoate, m. p. 55°; 1-naphthyl phenyl thioketone, m. p. 110°; diphenyl thioncarbonate, m. p. 106°; diphenyl trithiocarbonate, m. p. 98°; di(benzothiazol-2-yl) disulphide, m. p. 180·5°; di-1-thionaphthoyl disulphide, m. p. 167°; di(tetramethylthiuram) disulphide, m. p. 157° (decomp.).

Decalin was distilled from sodium, and passed through a column packed with silical gel previously activated *in vacuo* at 250°.

Spectra.—Extinction coefficients were measured with a Unicam SP 500 Spectrophotometer, fitted with a small electronically controlled (Vodden, *J. Soc. Chem. Ind.*, 1950, **69**, 51) thermostatic cell-compartment regulated to $\pm 0{\cdot}3°$. Water or glycol was used as bath-liquid; the latter gradually lost transparency at 100°, owing to dehydration to acetaldehyde. The solutions were examined in 1 cm. fused-quartz stoppered cells: a sealing agent was unnecessary except with ethanolic solutions, for which phosphoric oxide was used. (Silicone grease was extracted by the hot solution and affected the transmission at $\lambda < 2800$ Å.)

To eliminate the band-width of the spectrophotometer as a source of error the width of the slit was kept constant at a given wavelength, the sensitivity control being used to compensate the change in response of the photocell with temperature. The wavelength calibration of the instrument was affected by the conduction of heat from the thermostat and was standardised against a mercury or helium spectrum at each temperature; the correction at 100° was *ca.* 10 Å at 4359 Å, decreasing at shorter wavelengths. Solute concentrations *at the working temperature* were used to evaluate ε (l. mole^{-1} cm.$^{-1}$) from the readings of optical density. Except with di-1-thionaphthoyl disulphide, the extinction coefficients at room temperature were reproducible after one or more cycles of heating and cooling.

Appendix

The thermal shift is treated as a displacement of the whole absorption band (without change of shape) by $\Delta\nu$ along the frequency axis. If the band is approximated by a Gaussian function,

$$\varepsilon = \varepsilon_{max.} \exp(-x^2/2); \; x = (\nu_{max.} - \nu)/a_r \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

the frequency, ν_e, corresponding to $(\Delta\varepsilon)_{max.}$ is given by the expression,

$$\nu_e = \nu_{max.} - (a_r + \Delta\nu/2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(where $\nu_{max.}$ refers to the peak frequency of the absorption band before displacement) and the value of $(\Delta\varepsilon)_{max.}$, if $a_r \gg \Delta\nu$, is

$$(\Delta\varepsilon)_{max.} = 0{\cdot}6 \; \varepsilon_{max.} \; \Delta\nu/a_r \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

In practice, a different value of the parameter a is required for each wing of the absorption band. The red wing is chosen for comparison because it is influenced less by thermal broadening of the second transition; to emphasise this, the parameter a in equations (1)—(3) is specified by the subscript r. $\Delta\nu$ must be a function of the temperature change and presumably of the solvent also; but with the present measurements it is not possible to sort out these effects, and the values of ν_e and $(\Delta\varepsilon)_{max.}$ in columns 5 and 6 of Table 3 are evaluated from equations (2) and (3) with $\Delta\nu$ uniformly put equal to 100 cm.$^{-1}$.

Agreement between ν_e and the recorded frequency of $(\Delta\varepsilon)_{max.}$ (col. 2 of Table 3) is only qualitative, the recorded frequencies being on an average some 300 cm.$^{-1}$ to the red of ν_e.

According to (2), however, ν_c is independent of $\Delta\nu$ (provided a_r is $\gg\Delta\nu$) and therefore of temperature: that this condition is satisfied can be seen from Fig. 1 where the position of $(\Delta\varepsilon)_{max.}$ is unchanged at 60—115°. The values of $(\Delta\varepsilon)_{max.}$ calculated from (3) with $\Delta\nu$ = 100 cm.$^{-1}$ are all lower than the experimental, but this is deliberate and agreement would be

TABLE 3.

Compound *	$(\Delta\varepsilon)_{max.}$ ν (cm.$^{-1}$)	Intensity	a_r (cm.$^{-1}$)	$\Delta\nu$ = 100 cm.$^{-1}$ ν_c (cm.$^{-1}$)	$(\Delta\varepsilon)_{max.}$ (Calc.)
1-$C_{10}H_7$·CS·SMe (I)	19,100	14	900	19,500	8
1-$C_{10}H_7$·CS·Ph (II)	14,500	14	1100	15,050	8
$(PhO)_2CS$ (III)	28,500	3	1600	28,900	2
$(p$-MeO·C_6H_4·O$)_2CS$ (IV) ...	28,600	5	1400	28,650	3
$(PhS)_2CS$ (V)	20,300	7	1100	20,600	2

* The temperature range and the solvent are specified in Table 1.

reached with $\Delta\nu$ = 150 cm.$^{-1}$. The experimental values of $(\Delta\varepsilon)_{max.}$ include a (positive) contribution from the thermal broadening estimated, by inspection of the curves, at about one-third; the remaining two-thirds is attributed to the thermal red shift, and the preferred value of $\Delta\nu$ is therefore ~100 cm.$^{-1}$ with 150 cm.$^{-1}$ as an upper limit. The experimental peak frequencies do in fact change with temperature (Table 1) and the observed shifts are of this order; but it should be noted that the recorded values of $\nu_{max.}$ are not certain to within ±40 cm.$^{-1}$ and therefore that the direct observation of $\Delta\nu$ is subject to a considerable error.

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5. *Sedimentation Potentials. Part I. The Measurement of Sedimentation Potentials in Some Aqueous and Non-aqueous Media.*

By G. A. H. ELTON and J. B. PEACE.

An experimental study has been made of sedimentation potentials of glass particles in water and dilute aqueous potassium chloride, and of silica and glass particles in toluene and ether. The results for aqueous media have been used in a preliminary test of the theoretical equations of Smoluchowski and of Hermans. The potentials obtained in non-aqueous media appear to be electrostatic in origin, and cannot be interpreted on the basis of these electrokinetic equations.

ALTHOUGH sedimentation potentials were first investigated by Dorn (*Ann. Physik*, 1878, **3**, 20; *Wied. Ann.*, 1880, **10**, 46) over seventy years ago, the present state of knowledge concerning them is rather unsatisfactory. Theoretical considerations have been given by Smoluchowski (in Graetz's "Handbuch der Elektrizität und des Magnetismus," Leipzig, 1921, Vol. II, p. 385), by Hermans (*Phil. Mag.*, 1938, **26**, 650), and, more recently, by Booth (*J. Chem. Phys.*, 1954, **22**, 1956), but, as Booth points out, there are hardly any experimental results available with which to test the equations derived. The two most important experimental papers are those of Stock (*Anz. Akad. Wiss. Krakau*, 1913, *A*, 131; 1914, *A*, 95), who studied potentials set up by quartz particles sedimenting in toluene and in ether, and of Quist and Washburn (*J. Amer. Chem. Soc.*, 1940, **62**, 3169), who used Pyrex glass particles in water and in dilute aqueous solutions. The present paper describes work which confirms and extends the results of Quist and Washburn and may be used in a preliminary test of the theoretical equations given by Smoluchowski, Hermans, and Booth (*locc. cit.*). Stock's results for toluene and ether have been partially confirmed.

Experimental

Materials.—Ground Pyrex glass, sieved to the size range 95 ± 10 μ, and cleaned as described by Elton and Hirschler (*J.*, **1952**, 2953), was used to check the results of Quist and Washburn. Soft glass spheres, supplied by The English Glass Company, Ltd., were used in studies of the effect of particle radius on the sedimentation potential. Four batches of spheres, sieved to fairly uniform sizes (±7%), were used, the mean radii of the batches, determined microscopically, being (i) **51**, (ii) **112**, (iii) **216**, and (iv) **372** μ. For the experiments with toluene and ether, ground fused silica, sieved to the size range 20 ± 2 μ and cleaned as described by Dulin and Elton (*J.*, 1952, 286), was used.

The water used throughout these experiments was equilibrium conductivity water, prepared by an ion-exchange process, and was of specific conductivity $0{\cdot}8$—$1{\cdot}0 \times 10^{-6}$ ohm^{-1}. " AnalaR " potassium chloride was recrystallised several times from conductivity water. Ether was dried over calcium chloride and sodium, and redistilled; sulphur-free toluene was dried over potassium carbonate.

Apparatus and Technique.—Conductivities were determined on a conventional A.C. Wheatstone bridge.

The sedimentation cell used for the experiments with aqueous media was identical with that of Quist and Washburn (*loc. cit.*). Silver–silver chloride electrodes were prepared by Brown's method (*J. Amer. Chem. Soc.*, 1934, **56**, 646); the potentials were measured, earthed leads being used, on a valve millivoltmeter of standard design, being determined from measurements of the change in anode current; calibration of the instrument for various values of grid bias and circuit resistance was necessary. By suitably adjusting the grid bias of the valve it was possible to ensure that the current passing through the sedimentation cell during the taking of a measurement was less than 5×10^{-9} amp. Owing to the high internal resistance of the cell, readings were very sensitive to moisture in the air. The cell was therefore mounted inside an earthed metal box through which warm dry air was drawn during the experiment, and the voltmeter was housed in a dry, air-tight, earthed metal box, the controls being operated from outside. The 120-v battery supplying the high tension for the voltmeter was left on for several days before an experiment was started, in order to minimise voltage drift. With these precautions a sensitivity of 0·02 mv was obtained, the limiting factor generally being the stability of the electrodes.

The experimental technique was similar to that of Quist and Washburn (*loc. cit.*), except that the particles were previously equilibrated with the solution to be used by prolonged shaking. (This produced a rise in the specific conductivity of the solution.) The rate of flow of sedimenting particles could be adjusted by the operation of the tap leading from the reservoir of particles. A pointer moving over a scale was attached to the tap to facilitate the reproducing of flow rates, determined by the time taken for a known weight of powder to flow through the tap. The mass M per unit volume of suspension could then be calculated from the rate of flow and the velocity of sedimentation of the particles, determined in a separate experiment. The potential difference between any pair of the three electodes could be measured, and the steady value reached after the particles had been falling for a short time gave the sedimentation potential, after correction for any slight asymmetry potential present between the electrodes in the absence of falling particles.

The total potential difference measured in a given experiment was found to be directly proportional to the distance between the electrodes, indicating that the sedimentation field of the particles had become constant by the time that the top electrode had been reached. The measured potentials were found to be independent of the size of the silver–silver chloride electrodes used, agreement to within experimental error (±4%) being obtained with (*a*) wire electrodes of area 10^{-3} cm.^{2} or (*b*) plate electrodes of area 1 cm.^{2}. Other types of electrode tried, namely, of antimony and tungsten, proved unsatisfactory owing to lack of stability.

Suitable adjustment of the grid bias of the voltmeter made it possible to measure potentials in a given system while passing different currents. In all experiments it was found that the measured potentials were not affected, within experimental error, by varying the current passing between $2{\cdot}5 \times 10^{-9}$ and 3×10^{-8} amp.

The sedimentation cell used for the work on non-aqueous liquids was very similar to that used by Stock (*loc. cit.*). It consisted of a long Pyrex-glass tube of diameter 1·4 cm., fitted with a ground-glass joint at each end, and having two sealed-in platinum wire electrodes (each of area 5×10^{-4} cm.^{2}) 110 cm. apart. The potentials were measured with a quadrant electrometer, suitably connected, as described by Stock (*loc. cit.*). The silica powder was made to fall through the non-aqueous liquid simply by inverting the cell.

Results and Discussion

(a) *Aqueous Media.*—The experiments were carried out at room temperature, namely $20° \pm 6°$, and it was found that the sedimentation potential gradient, E, for a given system was independent of temperature over this range. For purposes of comparison of different systems it was found convenient to plot E as a function of $\kappa\eta$ (where κ is the specific conductivity and η is the viscosity of the liquid), which is also practically independent of temperature.

The Pyrex powder used was of the same size range as that used by Quist and Washburn (*loc. cit.*). It was confirmed that the sedimentation potential was directly proportional to M, the direction of the potential gradient indicating that the Pyrex particles were negatively charged. The Table gives the ratio E/M obtained by us for water and two aqueous solutions of potassium chloride, of measured conductivity after equilibration with the glass. Quist and Washburn (*loc. cit.*) do not give the conductivities of their

Solution	$10^6\,\kappa$ * (ohm^{-1})	$10^2\,E/M$ (v/g.)	ζ_1 (v)	ζ_2 (v)	ζ_3 (v)	ζ_4 (v)	ζ_5 (v)
10^{-4}N-KCl	14·6	7·6	0·14	0·14 †	0·24	0·24	0·12
10^{-5}N-KCl	3·0	35	0·14	0·10	0·23	0·17	0·13
Water	1·1	133	0·19	0·12	0·33	0·20	0·13

* The specific conductivity of the water used by Quist and Washburn was $1{\cdot}4 \times 10^{-6}$ ohm^{-1}. The specific conductivities of the salt solutions were not given, so it has been assumed, for the purpose of approximate comparison, that these were the same as ours.

† This value is likely to be less accurate than the rest of Quist and Washburn's results, as the results of only a few determinations are quoted, and these are rather scattered.

solutions of sodium chloride, but our results for E are in fairly good agreement with theirs at corresponding concentrations. Quist and Washburn calculated the electrokinetic potential ζ for water from their results for the non-spherical particles, assuming the applicability of Smoluchowski's equation (*loc. cit.*) for spherical particles. This equation is

$$E = \varepsilon\zeta g\,(\rho_2 - \rho_1)M/4\pi\kappa\eta\rho_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where ε is the dielectric constant in the diffuse part of the electrical double layer; g is the gravitational constant; and ρ_2, ρ_1 are the densities of the solid and solution respectively.

This equation was also obtained by Booth (*loc. cit.*) for the limiting case where the double-layer thickness is much smaller than the size of the particles, and the mobilities of all the ions are approximately equal. Both of these conditions are fulfilled by our systems. The Table also gives the values of ζ calculated from our results (ζ_1) and from those of Quist and Washburn (ζ_2) (*loc. cit.*) by using equation (1), and corresponding values ζ_3, ζ_4, obtained by using Herman's equation (*loc. cit.*), *viz.* :

$$E = 7\varepsilon\zeta g\,(\rho_2 - \rho_1)\,M/48\pi\kappa\eta\rho_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

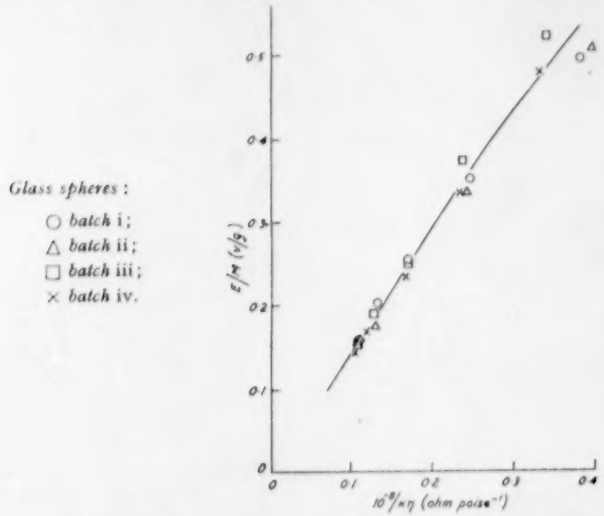
This equation, differing from (1) by the factor 7/12, takes into account the effect of relaxation forces, set up by the distortion of the electrical double layer, on the sedimentation potential.

Finally the Table gives, for comparison, ζ_5, the electrokinetic potential of Pyrex glass in dilute potassium nitrate solutions, calculated by Ghosh, Choudhury, and De (*Trans. Faraday Soc.*, 1954, **50**, 955) from the results of Wijga (Thesis, Utrecht, 1946). It is seen that agreement is reasonable between our results and those of Quist and Washburn, it being borne in mind that it was necessary to assume values for the conductivity of their solutions. The values of ζ calculated from equation (1) agree better with ζ_5 (from streaming potentials) than do those calculated from equation (2). We may therefore make the following tentative deductions. (*a*) The assumption that equations (1) and (2) may be applied to non-spherical particles is apparently not greatly in error. (*b*) If the above-mentioned assumption is exactly valid, then equation (1) appears to be more nearly correct than equation (2). Further discussion of this point is given below (p. 25).

Quist and Washburn did not investigate the effect of change of particle size on the measured potentials. Equations (1) and (2) both demand that the E.M.F. should depend

on the mass of particles per c.c. of suspension, but not on the particle size, so long as this is much greater than the double layer thickness. We have checked this, using soft glass spheres, of the four sizes mentioned above, in dilute aqueous potassium chloride. The glass was rather soluble in water, so in order to avoid the use of solutions of too high a conductivity, the spheres were leached many times with conductivity water before bringing them into contact with the solution to be used. In this way it was possible to ensure that no change in conductivity of the solution used occurred during the time necessary to carry out a run. The values of E/M for the four particle sizes are shown in the Figure as a function of $1/\kappa\eta$. Within experimental error all the points lie on a straight line of slope $0{\cdot}4_4 \times 10^9$ e.s.u. cm.^{2} sec.$^{-1}$, through the origin. We deduce, therefore, that E/M is independent of particle size. Furthermore, equations (1) and (2) both lead to the conclusion that ζ is approximately independent of ionic strength over the range considered ($\kappa = 3 \times 10^{-6}$ to 1×10^{-5} ohm^{-1}; $c \simeq 1$—7×10^{-5} N).

This is often observed for such extreme dilutions when silver–silver chloride electrodes are used [see, *e.g.*, Ghosh, Choudhury, and De (*loc. cit.*); Dulin and Elton (*loc. cit.*)].



Equation (1) gives $\zeta = 0{\cdot}08$ v, and equation (2) gives $\zeta = 0{\cdot}14$ v. As was the case for the Pyrex powder, equation (1) gives the more satisfactory value of ζ, which is usually found to be approx. 0·1 v for glass in very dilute aqueous solutions. We may take the results of these two sets of experiments as a preliminary indication that equation (1), due to Smoluchowski, is more satisfactory than equation (2), due to Hermans. Further tests are obviously necessary before final quantitative conclusions can be drawn. For these tests it will be desirable to experiment also with smaller particles than those used here, which show some deviation from Stokes's law, especially for the largest sizes. This effect does not, however, influence the agreement between the values of E/M found for the different particle sizes.

(b) *Non-aqueous Media.*—The results of the experiments with non-aqueous liquids were less satisfactory than of those with aqueous liquids. Despite careful precautions to purify and dry the liquids and to clean the silica particles, results were rather variable from day to day. The potentials, however, were of the same order as those obtained by Stock (*loc. cit.*), and the direction of E indicated the presence of a negative charge on the silica particles. A few runs were also done with soft glass spheres of radius $59 \pm 5\,\mu$, with similar lack of reproducibility. This is very probably due to the very low conductivity of the liquids, which made the effect almost purely electrostatic. Marked agglomeration of the particles also occurred, especially in the toluene, resulting in turbulent settling. When the cloud of particles was around one of the electrodes, a deflection was obtained on the

electrometer which did not depend on whether the other electrode was connected or not. When the cloud had passed the electrode there was an equally large deflection in the other direction, indicating that a positive ion atmosphere was situated behind the sedimenting particles. This counter deflection could not be due to an instrument effect as the same deflection was obtained if the electrode was not connected until immediately after the cloud of particles had passed it. Since the potential measured depended only on the number of particles around the electrode being used, and was independent of what was happening in the rest of the tube or near the other electrode, neither equation (1) nor equation (2) was applicable. It does not, therefore, appear profitable to investigate further the sedimentation potentials set up in non-aqueous liquids until our knowledge of those in aqueous solutions, to which equations of this type do apply, is more complete.

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6. *Cinnolines and Other Heterocyclic Types in Relation to the Chemotherapy of Trypanosomiasis. Part XI.* Some Reactions of Simple Quinoxaline Derivatives.*

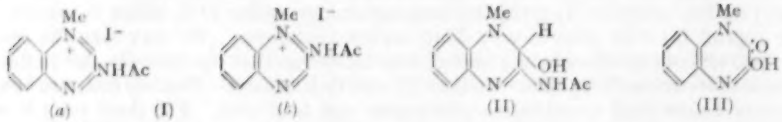
By C. M. Atkinson, C. W. Brown, and (the late) J. C. E. Simpson.

Quaternisation of 2-acetamidoquinoxaline has been shown to occur at position 4.

The orientation of the products from the reaction between 1 : 2-diamino-4-nitrobenzene with *n*-butyl glyoxylate has been established by comparison with derivatives of 7-amino-2-hydroxyquinoxaline.

In Part IX (*J.*, 1954, 2023) we described the synthesis of azoquinoxaline derivatives for conversion into potential trypanocides. The difficulties encountered in that work emphasised the importance of investigating the reactions of simple members of this series before proceeding with the bis-heterocyclic types. This paper describes some of these reactions.

2-Aminoquinoxaline was prepared both by acid-hydrolysis of alloxazine (cf. Wolf, Beutel, and Stevens, *J. Amer. Chem. Soc.*, 1948, **70**, 2572) and from the 2-hydroxy-derivative *via* the chloro- and the phenoxy-compound. The increased stability of these quinoxaline derivatives compared with corresponding members of the cinnoline and phthalazine series was evident from the much longer time required for phenoxylation and from the negligible yield of amine obtainable from 2-phenoxyquinoxaline and molten ammonium acetate; the chloro-compound was unchanged by refluxing with 0·1N-hydrochloric acid during two hours.



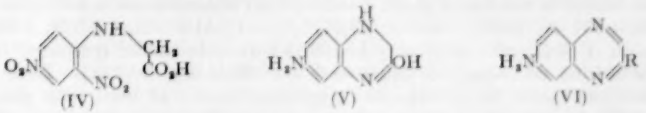
(*a*) (I) (*b*) (II) (III)

Attempts to quaternise 2-aminoquinoxaline gave discouraging results, the products being either intractable gums or solids which were obtained pure in only very low yield. However, 2-acetamidoquinoxaline reacted smoothly with methyl toluene-*p*-sulphonate; the product was isolated as the methiodide. Degradation of this by boiling alkali yielded one equivalent of ammonia and the sodium salt of (III) (cf. Usherwood and Whiteley, *J.*, 1923, 1039) which was converted into 2 : 3-dichloroquinoxaline by phosphorus pentachloride. Thus it appears that 2-acetamidoquinoxaline is quaternised at position 4 (cf. I*a*) and that atmospheric oxidation of the intermediate (II) takes place during the treatment with alkali. The alternative structure (I*b*) would yield 1-methyl-2-quinoxalone on treatment with alkali, and hydroxylation of this compound, necessary to provide (III), was shown not to occur under the conditions of the decomposition.

* Part X, *J.*, 1955, 4236.

The diminished reactivity of substituents in the hetero-ring of quinoxaline prompted a study of *Bz*-nitro-compounds which might also be used as models for reactions in the azoquinoxaline series. There appeared to be no known unambiguous synthesis of a *Bz*-nitroquinoxaline derivative. Wolf and his co-workers (*J. Amer. Chem. Soc.*, **1949**, **71**, 6) prepared mixed 2-hydroxy-6- and -7-nitroquinoxaline and separated the 2-chloro-derivatives which they designated "**6a**" and "**6b**." A simple method to determine the orientation of these isomers was suggested by the conversion of 2-(2 : 4-dinitroanilino)-ethanol into 2-(2-amino-4-nitroanilino)ethanol by Ramage and Trappe (*J.*, 1952, 4406). 7-Amino-3 : 4-dihydro-2-hydroxyquinoxaline was prepared by Waldmann (*J. prakt. Chem.*, 1915, **91**, 190) from 2 : 4-dinitrophenylglycine (IV) and it was expected that mono-reduction of this by Ramage's method would lead to 2-hydroxy-7-nitroquinoxaline; however, no definite product could be isolated. Wolf's "**6a**" series was shown to be identical with 7-nitroquinoxaline derivatives as follows.

Repetition of Waldmann's work showed that the quantities of tin and hydrochloric acid specified for the conversion of the acid (IV) into the dihydroquinoxaline were insufficient. In our hands the anhydrous base had m. p. *ca.* 280° (decomp.), compared with m. p. 181° reported by Waldmann, but was undoubtedly the required compound since oxidation yielded 7-amino-2-hydroxyquinoxaline (VI; R = OH). The ease with which this oxidation was effected with alkaline hydrogen peroxide or simply by boiling the dihydro-compound with water is in contrast to Waldmann's failure to oxidise his product with a variety of reagents. Treatment of the hydroxy-amine (VI; R = OH) with phosphorus oxychloride gave, at best, a poor yield of the chloro-compound (VI; R = Cl) which was only partially converted by prolonged treatment with potassium hydroxide in phenol into 7-amino-2-phenoxyquinoxaline (VI; R = OPh). This was identical with the compound formed from 2-chloro-"**6a**"-nitroquinoxaline by phenoxylation and subsequent catalytic reduction.



(IV) (V) (VI)

Confirmation of this identity was obtained by hydrolysis of 2-chloro-"**6a**"-nitroquinoxaline and subsequent reduction to yield a high-melting amino-hydroxy-derivative which was shown to be identical with (VI; R = OH) by paper chromatography and by comparison of the acetyl derivatives. This decision on the orientation of Wolf's "**6a**"-nitro-series is the only one to be taken, apart from the identification of the "**6a**"-methyl compounds as genuine 6-methylquinoxalines by Platt (*J.*, 1948, 1310).

Experimental

2-Hydroxyquinoxaline.—A solution of sodium toluene-*p*-sulphonate (1·7 g.) in N-sulphuric acid (8·4 c.c.) was dried (Dean and Stark trap) by refluxing with benzene (600 c.c.) for 5—6 hr. Tartaric acid (150 g.) and butan-1-ol (276 c.c.) were added and the mixture refluxed for 24 hr., the theoretical volume of water being collected. The mixture was washed with water and dilute alkali, benzene and excess of butanol were removed, and the residue was distilled, to yield di-*n*-butyl tartrate (239 g., 91%), b. p. 178—180°/14 mm., n_D^{18} 1·4474. This material (50 g.) was stirred vigorously with 0·402M-sodium periodate solution (475 c.c.) and ether-extracted, to provide by distillation pure *n*-butyl glyoxylate (43 g., 86%), b. p. 55°/14 mm., n_D^{18} 1·4443.

A mixture of *n*-butyl glyoxylate (2·5 g.), ethanol (20 c.c.), and *o*-phenylenediamine (2 g.) was refluxed for 2 hr., then cooled and 2-hydroxyquinoxaline (2·52 g., 94%), m. p. 267—269°, was collected; this was purified by dissolution in alkali, treatment with carbon, and precipitation with acid (2·35 g.; m. p. 268—270°).

2-Phenoxyquinoxaline.—Prepared as usual from the chloro-compound (1·75 g.; Gowenlock, Newbold, and Spring, *J.*, **1945**, **622**; isolation modified by pouring reaction mixture into iced sodium hydroxide solution and extraction with ether) and potassium hydroxide (0·72 g.) in phenol (7 g.) at 95° for 14 hr., *2-phenoxyquinoxaline* (2·23 g.), m. p. 100—101°, crystallised from

light petroleum (b. p. 60—80°) (Found: C, 75·85; H, 4·5; N, 12·65. $C_{14}H_{10}ON_2$ requires C, 75·65; H, 4·5; N, 12·6%).

2-Aminoquinoxaline.—A mixture of alloxazine (12 g.) and 80% (v/v) sulphuric acid (60 c.c.) was heated at 195—200° for 30 min., then cooled and poured on crushed ice (600 c.c.). After removal of insoluble green material the combined filtrates from this and two similar experiments (with 15 g. and 13 g. of alloxazine) were clarified with charcoal and basified with ammonia (*d* 0·880), and the yellow needles of 2-aminoquinoxaline (12 g., 45%), m. p. 151—153°, were collected.

Quaternisation of 2-Aminoquinoxaline.—(*a*) The base (0·46 g.) and methyl toluene-*p*-sulphonate (0·65 g.) were heated at 105° until the red melt became much more viscous (7 min.), then cooled, water (5 c.c.) was added, and the filtrate (from a trace of solid) was extracted with ether to remove excess of ester. Addition of saturated potassium iodide (equal volume) slowly gave a black solid (0·5 g.), m. p. 190—205°. Digestion of this with hot water left an insoluble fraction (0·02 g.), m. p. 248—251°, and there separated from the filtrate the dark red *methiodide* (0·09 g.), m. p. 185—187° raised to 188° by two recrystallisations from water (Found: C, 36·1; H, 3·9; N, 12·2; I, 40·9. $C_9H_{10}N_2I$ requires C, 36·5; H, 3·7; N, 14·2; I, 42·9%).

2-Acetamidoquinoxaline Methiodide.—The base (5 g.) and methyl toluene-*p*-sulphonate (5 g.) were heated at 100—110° for 30 min. (the melt solidified). The mixture was dissolved in water (75 c.c.), and the *iodide* (7·4 g.), m. p. 328—340° (decomp.), isolated as above and recrystallised from water to provide red needles (5·8 g.), m. p. 343—344° (decomp.) (Found: C, 40·35; H, 3·7; N, 13·7; I, 34·8. $C_{11}H_{13}ON_3I$ requires C, 40·1; H, 3·7; N, 12·75; I, 38·5%).

Alkaline decomposition. A solution of the salt (2 g.) in water (180 c.c.) was refluxed with 40% aqueous sodium hydroxide (29·5 c.c.) in a Kjeldahl apparatus through which nitrogen passed. After 1½ hr., one equiv. of ammonia had been evolved and the solution was concentrated in a desiccator. A sodium salt (0·7 g.), m. p. 360°, separated from 90 c.c. and further concentration to 40 c.c. gave more solid (0·6 g.), m. p. *ca.* 300°. Acidification of the former material (0·2 g.) with concentrated hydrochloric acid gave a solid (0·154 g.), m. p. 261—267°, which separated as colourless needles, m. p. 287·5—288°, from nitromethane or 2-ethoxyethanol (Found: C, 61·5; H, 4·35; N, 15·95. Calc. for $C_9H_8O_2N_2$: C, 61·4; H, 4·6; N, 15·9%). This was identical with 1:2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (prepared from *N*-methyl-*o*-phenylenediamine according to Usherwood and Whiteley, *loc. cit.*). Both materials gave 2:3-dichloroquinoxaline, m. p. 145—148°, on reaction for 15 min. with phosphorus pentachloride at 160°, decomposition with water, and recrystallisation from aqueous ethanol.

7-Amino-3:4-dihydro-2-hydroxyquinoxaline (cf. Waldmann, *loc. cit.*).—2:4-Dinitrophenylglycine (10 g.; m. p. 205—206°) and granulated tin (30 g.) were treated with portions of concentrated hydrochloric acid (total, 100 c.c.), with cooling towards the end of the addition. After 2 hours' heating on a steam-bath the solution was diluted with water (750 c.c.) and filtered and tin salts were removed by hydrogen sulphide. The precipitated sulphides were digested three times with boiling water (total, 750 c.c.), and the combined digests and filtrate were evaporated to a small volume. Colourless needles of the dihydrochloride (8 g., 82%) which separated overnight were washed with ethanol and ether and dissolved in the minimum volume of hot water, and crystalline sodium acetate (8 g.) was added. The dihydrate of the base was collected and recrystallised from water, from which it formed yellow cubes (5·7 g.), m. p. 288° (decomp.). Heating the dihydrate (1·0 g.) for 3—4 hr. at 130—140° yielded the anhydrous base, m. p. 288° (decomp.). This (0·4 g.) was refluxed for 30 min. with acetic anhydride (2 c.c.), and the cold mixture diluted with ether. The yellow solid (0·42 g.), m. p. 290—295° (decomp.), was recrystallised twice from formamide; the pure brownish-yellow *diacetyl derivative* had m. p. 294—295° (decomp.) (Found: C, 58·7; H, 5·55; N, 17·6. $C_{12}H_{13}O_3N_3$ requires C, 58·3; H, 5·3; N, 17·0%).

7-Amino-2-hydroxyquinoxaline.—A solution of the foregoing dihydrate (10 g.) in 2N-sodium hydroxide (105 c.c.) was heated on a steam-bath for 30 min. with 3% aqueous hydrogen peroxide (95 c.c.). The hot, dark red solution was filtered and acidified with acetic acid, and the crude solid (7·2 g.), m. p. 360°, collected. Pure *7-amino-2-hydroxyquinoxaline*, m. p. 360°, was obtained by recrystallisation from nitrobenzene (Found: C, 59·45; H, 4·4; N, 26·4. $C_8H_7ON_3$ requires C, 59·61; H, 4·4; N, 26·1%).

7-Amino-2-chloroquinoxaline.—The hydroxy-compound (2 g.) was heated on the steam-bath for 15 min. with phosphoryl chloride (10 c.c.), and the mixture poured on ice (300 c.c.) and 2N-sodium hydroxide (300 c.c.). The washed, dried, and clarified (carbon) ethereal extract was evaporated to dryness under reduced pressure and the residue of yellow needles (0·37 g.; m. p. 200—201°) was recrystallised from chloroform to provide the *chloro-compound*, m. p. 200—201°

(Found: C, 53·65; H, 3·35; N, 23·65; Cl, 19·95. $C_8H_4N_2Cl$ requires C, 53·48; H, 3·37; N, 23·4; Cl, 19·73%).

7-*Amino*-2-*phenoxyquinoxaline*.—The foregoing chloro-compound (0·2 g.) was heated on a steam-bath for 16 hr. with potassium hydroxide (0·08 g.) in phenol (1 g.), and the mixture poured into 2N-sodium hydroxide. The suspension was extracted with ether, and the extract washed with 2N-sodium hydroxide and water, dried ($MgSO_4$), and evaporated to give a crude product (0·22 g.), m. p. 115—150°. Recrystallisation from chloroform gave unchanged material (20 mg.) but addition of light petroleum (b. p. 60—80°) to the chloroform mother-liquor produced crystalline material (0·11 g.), m. p. 125—127°, on storage overnight. The *phenoxy-compound*, m. p. 126—128°, separated from chloroform–light petroleum (b. p. 60—80°) in golden needles (Found: C, 70·9; H, 4·9; N, 17·8. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·7; N, 17·7%).

7-*Acetamido*-2-*hydroxyquinoxaline*.—A suspension of 7-amino-2-hydroxyquinoxaline (0·5 g.) in acetic anhydride (5 c.c.) was refluxed for 1 hr., then diluted with ether, and the solid (0·565 g.), m. p. 344—346° (decomp.), was collected. Recrystallisation from boiling nitrobenzene (500 parts) provided the *acetamido-compound*, m. p. 348—350°, as pale yellow needles (Found: C, 59·15; H, 4·2; N, 20·5. $C_{10}H_9O_2N_3$ requires C, 59·1; H, 4·5; N, 20·7%). This material was identical (mixed m. p.) with that prepared by acetylation of the "6a"-amino-hydroxyquinoxaline.

2-*Chloro*-6- *and* -7-*nitroquinoxaline*.—1 : 2-Diamino-4-nitrobenzene (9·2 g.; 197—198°) in 95% ethanol (72 c.c.) and *n*-butyl glyoxylate (8·7 g.) were refluxed with stirring for 2 hr., then cooled and filtered, and the mixed hydroxy-compounds (10·9 g.), m. p. 245—255°, washed and dried. This material (4 g.) was heated with phosphoryl chloride (40 c.c.) and phosphorus pentachloride (8 g.) on a steam-bath for 1 hr. and the clear brown solution was poured on crushed ice (800 c.c.). The solid (3·8 g.; m. p. 160—165°) was washed with sodium hydrogen carbonate solution (200 c.c.) and water, and dried in a desiccator over sodium hydroxide (the solid must be acid-free to prevent resinification during recrystallisation). Two recrystallisations from benzene gave pale yellow needles of 2-chloro-"6a"-nitroquinoxaline (1·65 g.), m. p. 185—186° (Wolf *et al.*, *loc. cit.*, give m. p. 184—186°); the mother-liquors gave colourless needles (0·2 g.), m. p. 158—160°, after concentration and repeated recrystallisation from benzene–light petroleum (b. p. 60—80°) (Wolf *et al.* give m. p. 160—161° for their "6b" isomer).

2-*Hydroxy*-"6a"-*nitroquinoxaline*.—The chloro-compound (1 g.; m. p. 185—186°) was refluxed for 2½ hr. with N-hydrochloric acid (20 c.c.) and ethanol (5 c.c.), and the suspension cooled. The 2-*hydroxy-compound* (0·82 g.) had m. p. 275—276°, unchanged by recrystallisation from nitromethane from which it separated in orange needles (Found: C, 50·05; H, 2·85; N, 22·45. $C_8H_5O_3N_3$ requires C, 50·3; H, 2·6; N, 22·0%).

"6a"-*Amino*-2-*hydroxyquinoxaline*.—A suspension of finely powdered 2-hydroxy-"6a"-nitroquinoxaline (0·4 g.) in glacial acetic acid (3 c.c.) was treated with the "stannous chloride–acetic anhydride reagent" of Albert and Linnell (*J.*, 1936, 1617) (8 c.c.). The red mixture, which was formed with much evolution of heat, was set aside for 50 min., poured into water (20 c.c.), and filtered. The hot filtrate was freed from tin, and the filtrate evaporated to dryness. "6a"-Amino-2-hydroxyquinoxaline (0·14 g.), m. p. 360°, was isolated as a yellow granular solid by dissolution of the dry residue in 2N-sodium hydroxide, treatment with carbon, and acidification with acetic acid. The amino-compound, more of which (0·08 g.) was obtained by digestion of the tin sulphides with hot water (30 c.c.), had the same solubility characteristics as 7-amino-2-hydroxyquinoxaline (above).

"6a"-*Nitro*-2-*phenoxyquinoxaline*.—2-Chloro-"6a"-nitroquinoxaline (1 g.) was heated on a steam-bath with a solution of potassium hydroxide (0·3 g.) in phenol (5 g.) for 2½ hr., then poured into 2N-sodium hydroxide (*ca.* 100 c.c.), and the solid product was collected in ether. Washing, drying ($MgSO_4$), treatment with charcoal, and evaporation gave a product (0·82 g.), m. p. 80—85°. Recrystallisation from light petroleum (b. p. 60—80°) yielded the *phenoxy-compound* (0·42 g.), m. p. 105—106° unchanged by further recrystallisation, as colourless needles (Found: C, 62·85; H, 3·3; N, 15·9. $C_{14}H_9O_3N_3$ requires C, 62·9; H, 3·4; N, 15·7%).

Attempted phenoxylation of the chloro-compound (0·1 g.) with phenol (0·3 g.) and ammonium carbonate (0·1 g.) on a steam-bath for 0·5—15 hr. gave only unchanged material (0·07 g.), 184—185°.

"6a"-*Amino*-2-*phenoxyquinoxaline*.—A solution of the foregoing nitro-compound (0·38 g.) in ethanol (75 c.c.) was shaken with platinum oxide (0·02 g.) and hydrogen at 1 atm. until absorption ceased (2½ hr.). Filtration and concentration under reduced pressure yielded a product (0·315 g.), m. p. 110—115°. Removal of some ether-insoluble impurity and two crystallisations from chloroform–light petroleum (b. p. 60—80°) provided the amine (0·095 g.)

as golden-yellow needles, m. p. 128—129° not depressed on admixture with 7-amino-2-phenoxyquinoxaline (above).

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7. *Ionophoresis of Carbohydrates. Part III.* Behaviour of Some Amylosaccharides and their Reaction with Borate Ions.*

By A. B. Foster, Miss P. A. Newton-Hearn, and M. Stacey.

Paper ionophoresis of a wide range of amylosaccharides has been studied using alkaline borate and other buffers. Amylose and amylopectin were found to have a characteristic behaviour and could be separated from each other. Evidence is presented which indicates that, in addition to known reactions (Part II *), borate ions appear to react in a unique manner with certain amylosaccharides. Application of paper ionophoresis to the *Neisseria perflava* polysaccharide (Barker, Bourne, and Stacey, *J.*, 1950, 2884) and to the synthetic amylosaccharides obtained by the action of mixtures of potato P- and Q-enzyme on D-glucose 1-phosphate (Barker, Bourne, Peat, and Wilkinson, *J.*, 1950, 3022) has provided additional information on the structure of these polysaccharides. The reaction of polyglucosans with borate ions is commented on.

The migration of acidic polysaccharides in paper ionophoresis has been studied in some detail (Rienits, *Biochem. J.*, 1953, **53**, 79; Pasternak and Kent, *Research*, 1952, **5**, 486; Greenway, Kent, and Whitehouse, *Research*, 1953, S 6; Ricketts, Walton, and Saddintgon, *Biochem. J.*, 1954, **58**, 532; cf. Gardell, Gordon, and Åqvist, *Acta Chem. Scand.*, 1950, **4**, 907) but only brief reports of the examination of neutral polysaccharides by this technique have been made (Greenway *et al.*, *loc. cit.*; Tiselius and Flodin, *Adv. Protein Chem.*, 1953, **8**, 461; Michl, *Monatsh.*, 1952, **83**, 737; Preece and Hobkirk, *Chem. and Ind.*, 1955, 257). The electrophoretic behaviour of amylosaccharides in agar jelly in the presence of iodine–iodide has been studied in detail by Mould and Synge (*Biochem. J.*, 1954, **58**, 585).

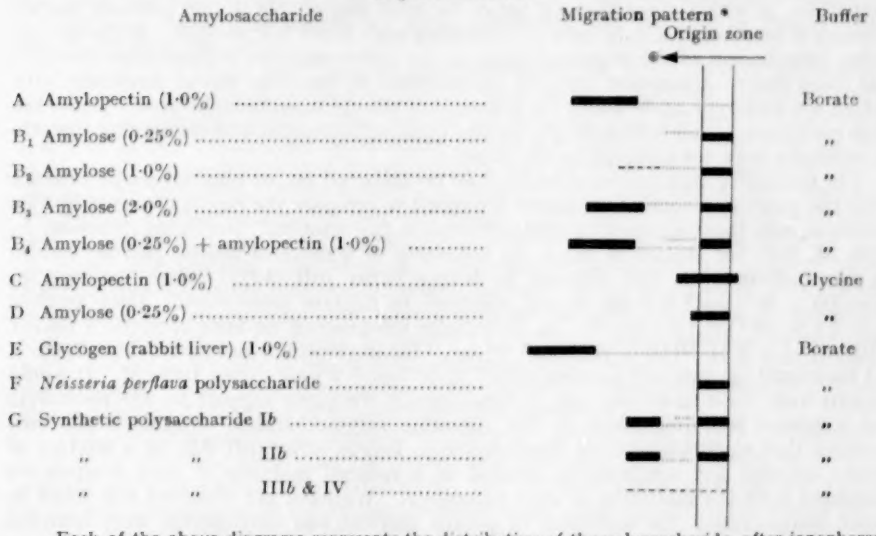
Migration of certain carbohydrate derivatives, in paper ionophoresis, is facilitated by the formation of negatively charged complexes with the borate ions present in the aqueous alkaline media employed as the conducting solution (see Part II and the references cited therein). The aims of this investigation were to examine the reaction of neutral polysaccharides with borate ions in the light of knowledge of the reactions which occur with mono- and oligo-saccharides (Part II) and to evaluate the paper electrophoresis of neutral polysaccharides.

In preliminary experiments potato amylose (B.V. 1·35) and amylopectin (B.V. 0·18) were examined ionophoretically in a borate buffer (pH 10; cf. Foster, *J.*, 1953, 982) under standard conditions (see Experimental section). The amylosaccharides could be detected on the neutralised paper by spraying it with ethanolic iodine. The amylopectin appeared as a reddish-brown zone and the amylose as a violet zone, as might be expected from the well-known nature of the complexes of these polysaccharides with iodine in solution. This method of detection was found to be specific for the amylosaccharides. Alternatively the iodine-vapour method of Brante (*Nature*, 1949, **163**, 651) as applied to polysaccharides by Greenway *et al.* (*loc. cit.*) may be employed; this method has been claimed as able to detect a range of polysaccharides (Greenway *et al.*, *loc. cit.*). Some of the results obtained are represented diagrammatically (A, B_1, B_2, B_3, B_4) in Table 1, from which it may be seen that whilst the amylopectin underwent appreciable migration toward the anode, with

* Part II, *J.*, 1955, 1778.

little absorption of the polysaccharide on the paper in the path of migration, the pattern of the amylose movement depended on the amount of the polysaccharide introduced on to the paper (cf. Greenway *et al., loc. cit.*). Thus, when a small amount of amylose was introduced on to the paper and subjected to ionophoresis, it was largely absorbed at the origin, although there was slight migration toward the anode (B_1). The strong absorption on the paper of the amylose in ionophoresis is not surprising since it has long been known

TABLE 1. *Diagrammatic representation of the ionophoretic migration of some amylosaccharides.*



Each of the above diagrams represents the distribution of the polysaccharide, after ionophoresis under standard conditions (see Experimental), in a cross-section of the paper perpendicular to its plane and parallel to the direction of the electric field.

* Representation of zones: —— main zone of polysaccharide, – – – – intermediate amounts of polysaccharide, ····· traces of polysaccharide. The figures in parentheses refer to the concentrations of the aqueous solutions of the polysaccharide introduced on to the paper (see Experimental).

that amylose is absorbed on cotton cellulose (see Gilbert, Greenwood, and Hybart, *J.*, 1954, 4454, and references cited therein). It might be expected that there would be a limit to the number of amylose molecules that can be absorbed per unit area of paper. Below this limit, as was observed in practice, no migration of the amylose would be expected to occur, and, above the limit, the extent of migration would be expected to depend on the amount of amylose introduced on to the paper. This is borne out by the patterns of movement B_1, B_2, and B_3. There was appreciable absorption of the amylose on the paper in the path of movement. The retention of a considerable amount of amylose at the origin zone in B_1, B_2, B_3, and B_4 may have been due to some irreversible absorption of the polysaccharide on the paper when the aqueous solutions of amylose were introduced on to the paper. The pattern of migration B_4 reveals that the mobility of amylopectin is not influenced by the presence of amylose.

In order to assess the influence of borate ions on the movement of amylose and amylopectin in ionophoresis, the behaviour of these polysaccharides in phosphate (pH 10·0) and glycine (pH 11·0) buffers was examined. From Table 1 (C and D) it may be seen that in glycine buffer the amylose remained largely absorbed at the origin whilst the amylopectin underwent slight migration toward the anode but much less than in borate buffer (the amount of amylose introduced on to the paper in B_1 and D was identical, as was the amount of amylopectin in A and C). The behaviour of amylose and amylopectin in phosphate

buffer was similar to that in glycine buffer. That there was true migration of the amylopectin in the non-borate buffers was supported by the fact that the slight migration occurred toward the anode, *against* the electroendosmotic flow. This slight movement may have been due to the presence of phosphate groups in the amylopectin and/or the formation of complexes between phosphate ions or glycine molecules with amylopectin (evidence which appears to support this will be described later). The migration of amylose in ionophoresis in borate buffer is undoubtedly due to complex formation with borate ions.

Ionophoresis of amylose samples with D.P. >4000, 415, and 135 showed that, in each case, there was considerable absorption at the origin. The molecular size of amylosaccharides at which absorption on paper becomes appreciable is not precisely known although it would appear to be between the rather wide limits D.P. 6—135. In the glycine buffer, ionophoresis of the oligosaccharides in the series maltose—maltohexaose revealed that there was no absorption, since all the members of the series moved identically with methyl α-D-xylopyranoside under the influence of the electroendosmotic flow. Under the same conditions α- and β-Schardinger dextrin (*cyclo*maltohexoside and *cyclo*maltoheptoside respectively) were not absorbed on the paper.

The possibility that polysaccharides may be absorbed on, or may otherwise interact with, the paper in ionophoresis, makes it difficult to compare the results obtained by this technique with those obtained by electrophoresis in free solution. Northcote (*Biochem. J.*, 1954, **58**, 353) has studied in detail the behaviour of a range of neutral polysaccharides on electrophoresis in free solution in borate buffer (pH 9·2). Potato amylopectin ($\mu = 3{\cdot}6 \times 10^{-5}$ cm.^{2} v^{-1} sec.$^{-1}$) was observed to migrate more rapidly than amylose ($\mu = 3{\cdot}1 \times 10^{-5}$ cm.^{2} v^{-1} sec.$^{-1}$). In filter-paper ionophoresis we have observed a similar relation: $\mu = 0{\cdot}51$—$0{\cdot}69 \times 10^{-6}$ cm.^{2} v^{-1} sec.$^{-1}$ for amylopectin, and for amylose (Table 1, B_3) the migrating zone had $\mu = 0{\cdot}35$—$0{\cdot}57 \times 10^{-6}$ cm.^{2} v^{-1} sec.$^{-1}$ (see Table 3). It would appears from these mobilities that, in ionophoresis, the paper support for the electrolyte has a general retarding effect on the migrating polysaccharides. Northcote (*loc. cit.*) reported that electrophoresis, in free solution in borate buffer (pH 9·2), of a mixture of potato amylose and amylopectin resulted in a reduced mobility of both components compared with the migration of each separately. We have not observed this effect in paper ionophoresis; the mobilities of potato amylose and amylopectin were identical when the polysaccharides were run separately or in admixture (Table 1, B_4).

It is conceivable that the absorption of polysaccharides on the paper in ionophoresis may be used to advantage in certain cases, as, for example, in the separation of amylose and amylopectin, by controlling the amount of the amylose introduced on to the paper. On the other hand, a possible disadvantage that might arise is the difficulty in assessing accurately the intensity of reaction of a polysaccharide with borate ions (which is essential for information on polysaccharide structure) if appreciable absorption occurs.

Several attempts to reduce the absorption of amylose in paper ionophoresis were made. Tiselius and Flodin (*loc. cit.*) report that the inclusion of anionic and neutral detergents in the buffer solution reduced the absorption of certain proteins in paper electrophoresis. Introduction of Teepol (mixed sodium alkanesulphonates) into the alkaline borate buffer almost completely prevented the migration of amylose and amylopectin. The reason for this action is at present unknown. Dissolution of amylose or amylopectin in molten urea (Clark, *Nature*, 1951, **168**, 876), followed by paper ionophoresis in alkaline borate or in alkaline borate containing 10% of urea, of an aqueous solution of the melt resulted in substantially slower migration of the polysaccharides. Ionophoresis of untreated amylose in borate buffer containing 40% of urea resulted in considerably reduced absorption of the polysaccharide. An amount of amylose (0·25% aqueous solution) which gave the migration pattern B_1 (Table 1) in alkaline borate gave a migration pattern similar to B_3 in the borate–urea buffer. The migration pattern of the amylopectin was not appreciably changed under these conditions. Conditions were not discovered whereby absorption of the polysaccharides could be eliminated completely. The high percentage of urea in the buffer system did not interfere seriously with the detection of the polysaccharides.

The blue values of the amylose and amylopectin (1·35 and 0·18 respectively) described above, indicated that each should contain a trace of the other. It was observed that in the

borate–urea buffer, where the coloration of the polysaccharides with iodine appeared to be intensified, ionophoresis of amylopectin revealed the presence of a small amount of intensely blue-staining material (most probably amylose) remaining at the origin. In the case of amylose a reddish zone (amylopectin) could be distinguished clearly, migrating just ahead of the amylose (the properties of amylose and amylopectin after ionophoresis will be described in a subsequent paper). Ethanolic iodine was used in these detections. In the normal borate buffer, ethanolic iodine did not reveal the traces but the iodine vapour method was effective in this respect. Thus, ionophoresis would appear to offer a means of checking the purity of amylose and amylopectin preparations. It should be emphasised that, since the method for the detection of amylopectin is considerably less sensitive than for amylose, precautions should be taken concerning the amounts of polysaccharide introduced on to the paper.

In Part II, evidence was presented which indicated that, in the alkaline media used in ionophoresis, borate ions reacted exclusively with the 4 : 6-hydroxyl groups in methyl α- and β-D-glucopyranoside. Thus in the amylosaccharides, which are 1—4α-linked, reactions of this type should occur solely at the non-reducing chain ends of the polysaccharide. On analogy with 4-*O*-methyl-D-glucose (M_G value 0·24; see Foster, *loc. cit.*) the reducing ends of the chains would be expected to react with borate ions. Because of the greater number of non-reducing end groups, amylopectin, on reaction with borate ions, would be expected to acquire a greater net negative charge, and hence to have a higher electrophoretic mobility than amylose. The contribution to the net negative charge, from borate-ion reaction with the reducing chain ends, would be expected to be the same for amylose and amylopectin since there is only one reducing end group per molecule in both polysaccharides. Glycogen, because of its shorter average chain length, and consequent greater percentage of non-reducing end groups per molecule, would be expected to migrate more rapidly than amylopectin in ionophoresis. These predictions are borne out by the results in Table 1 and by those of Northcote (*loc. cit.*).

The rate of migration of amylose is, however, greater than might be expected in view of its very long chain and the assumption that only the D-glucose units at the ends of the chains react with borate ions. Thus, other, hitherto unrecognised, reactions of the polysaccharide with borate ions probably occur. The well-known tendency for the helical chains of amylosaccharides to entrap other molecules, *e.g.*, iodine, butanol, etc., within the helices suggests that borate ions might be entrapped in a similar manner, thus conferring a negative charge on the molecule (cf. Mould and Synge, *loc. cit.*). Although direct proof of this could not be obtained some support was provided by the fact that α- and β-Schardinger dextrin were found to undergo appreciable migration on ionophoresis in borate buffer (Table 3). Reaction of individual D-glucose units in the cyclic dextrins is precluded (cf. Part II).

Ionophoresis of amylosaccharides may, in certain cases, provide information on their structure in addition to that obtained by other methods, for example, in the case of the amylosaccharides obtained by the action of variously composed mixtures of P- and Q-enzymes (from potatoes), on D-glucose 1-phosphate (Barker, Bourne, Peat, and Wilkinson, *J.*, 1950, 3022; Barker, Bourne, and Wilkinson, *J.*, 1950, 3027).

A series of polysaccharides were prepared which in certain cases (low Q : P ratio) could be separated into fractions which were soluble in water. The water-soluble fractions I*b*, II*b*, and III*b* (Barker *et al.*, *loc. cit.*), which had blue values 0·82, 0·44, and 0·22 respectively, were examined ionophoretically. With higher Q : P ratios, fractions were obtained which were completely soluble in water, *e.g.*, IV (B.V. 0·15). It was inferred from detailed studies by Barker *et al.* (*loc. cit.*) that there was a gradation of properties from amylose-type to amylopectin type polysaccharides as the Q : P ratio increased. Further, certain fractions, *e.g.*, I*b*, were dissimilar to any fractions isolatable from natural starch. Ionophoresis was found to reveal other differences between these polysaccharides and the components of natural starch. Polysaccharides I*b* and II*b* were found to contain two components with ionophoretic behaviour and staining properties with iodine similar to those of potato amylose and amylopectin (Table 1, A and B_1) but they migrated more slowly. Polysaccharide II*b* contained less of the amylose type component than I*b*. The

polysaccharides III*b* and IV exhibited unusual diffuse migration (Table 1, G), not previously encountered with amylosaccharides, and gave a reddish stain with iodine. Ionophoretically the polysaccharides III*b* and IV would seem to be somewhat different from natural amylopectin. It is of interest that the operation of an artificial mixture of P- and Q-enzymes on D-glucose 1-phosphate produces a range of polysaccharides whereas the naturally operating enzymes tend to produce the two distinct types, amylose and amylopectin.

Ionophoresis of the polysaccharide elaborated by *Neisseria perflava* revealed an unusual behaviour. The structure of this polysaccharide has been studied in detail (Barker, Bourne, and Stacey, *J.*, 1950, 2884; Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 994) and it has been recognised as of the glycogen type with an average chain length of 11—12 units. In ionophoresis it was found to remain stationary at the origin and gave a migration pattern (Table 1, F) very different from that of rabbit-liver glycogen (Table 1, E). Ionophoresis of a range of glycogens, *viz.*, ox liver, hog round worm, bee drone larvæ, bass liver, human liver, sheep tapeworm, dog liver, frog liver, chicken liver, guinea-pig liver, northern-pike liver [samples very kindly supplied by Professor F. Smith and described by Abdel-Akher and Smith (*loc. cit.*)] revealed a general behaviour essentially similar to that of rabbit-liver glycogen (Table 1, E). A detailed study of the electrophoretic behaviour of these glycogens will be published elsewhere (Professor F. Smith, personal communication). The ionophoretic behaviour of the *N. perflava* polysaccharide, as a glycogen-type polysaccharide, would therefore appear to be anomalous. The *N. perflava* polysaccharide has been observed to have a surprisingly low activating power in the conversion of amylose into amylopectin by the Q-enzyme isolated from *Polytomella coeca* (Barker, Bebbington, and Bourne, *J.*, 1953, 4051). It was suggested (Barker *et al.*, *loc. cit.*) that this might be due to the entanglement of the chains of the polysaccharide since the activating power depends on non-reducing chain ends. The behaviour of the *N. perflava* polysaccharide in ionophoresis would indicate either that the polysaccharide does not react with borate ions because of its structure or because of steric hindrance, or that it is strongly absorbed on the paper. Since the molecule appears to be of the glycogen type (Barker *et al.*, *loc. cit.*; Abdel-Akher and Smith, *loc. cit.*), and since in ionophoresis in non-borate buffers it did not migrate under the influence of the electroendosmotic flow, it appears that absorption is taking place. Since no measurement of the molecular weight of the polysaccharide has been made, the origin of any absorption effects is obscure at present.

Whilst the ability of borate ions to form complexes with carbohydrates is well known, there is little evidence to show that phosphate groups may behave similarly. When using alkaline non-borate buffers for comparison purposes, it was observed that members of the series maltose–maltohexaose and α- and β-Schardinger dextrin moved only under the influence of the electroendosmotic flow and identically with methyl α-D-xylopyranoside (cf. Part II) in glycine buffer (pH 11·0). In phosphate buffer (pH 10·0), however, all these compounds migrated toward the anode, with respect to methyl α-D-xylopyranoside. Although the precise origin of the migrations in phosphate buffer is unknown the results indicate that care should be taken in assessing the migration of carbohydrates in phosphate buffers in ionophoresis (cf. Goldwasser and Mathews, *J. Amer. Chem. Soc.*, 1955, **77**, 3135).

In considering the behaviour of polyglucosan in paper ionophoresis it appears that at least three factors must be taken into account: (1) solubility in the buffer solution, (2) absorption on the paper, and (3) mode of reaction with borate ions.

Clearly, paper ionophoresis can be applied only to polysaccharides which are soluble in the buffer system. Some aspects of absorption effects have been discussed above. The reaction of polyglucosans with borate ions is dependent upon the structure of the polysaccharide and two types of complex formation have been observed which involve (1) individual D-glucose residues and (2) D-glucose residues in different parts of the same molecule. No evidence has been obtained which suggests that more than one carbohydrate molecule can simultaneously react with a borate ion. Reaction of borate ions with D-glucose units within the polysaccharide chains would be expected to occur only if both the 4- and the 6-hydroxyl group are unsubstituted (cf. Part II). The reaction will be influenced

by the configuration of the glycosidic links along the polysaccharide chain. For polysaccharide chain ends, reaction with borate ions will be controlled, at the non-reducing end, by the configuration of the glycosidic linkage attaching it to the polysaccharide chain (Part II) and, at the reducing end, by the point of attachment of the remainder of the polysaccharide (cf. Part I, *J.*, 1953, 982). Reaction of the borate ions with D-glucose units in different parts of the same molecule will depend on the shape of the polysaccharide molecule and this appears to be especially favoured in the amylosaccharides.

A consideration of the ionophoretic behaviour of other neutral polysaccharides is reserved for a future communication.

Experimental

General Procedure for the Ionophoresis of Polysaccharides.—Whatman No. 3 paper was used throughout, although no significant differences were observed when No. 3MM paper was used. The technique for the preparation of the paper has been described in detail elsewhere (Foster, *Chem. and Ind.*, 1952, 1050). The amylosaccharides were introduced on to the paper in a rectangular zone of width 0·7 cm. (parallel to the direction of the applied electric field) and of optional length, by a single application of the appropriate amylosaccharide solution, from a capillary tube. The width of the rectangle corresponds to the origin zone in Table 1. Aqueous solutions of the polysaccharides were used and it was important to ensure that the spots of polysaccharide introduced on to the paper were kept moist. This precaution materially reduced the absorption of certain polysaccharides, especially amylose. If necessary the preparation of the paper may be reversed in that it is first soaked in the buffer solution, and blotted so that the origin line is surrounded by a dry zone on to which the solutions of polysaccharides may be introduced.

For the apparatus previously described (Foster, *loc. cit.*) the standard conditions adopted for the ionophoreses were 500 v for 4 hr. (final current 24 milliamp. for borate buffer).

Buffer Solutions.—The compositions of the buffer solutions employed in ionophoreses were as follows.

(a) *Borate* (pH 10·0): boric acid (7·44 g.) and sodium hydroxide (4·0 g.) per l. of solution.

(b) *Glycine* (pH 11·0): glycine (4·503 g.), sodium chloride (3·505 g.), and sodium hydroxide (1·8 g.) per l. of solution.

(c) *Phosphate* (pH 10·0): disodium hydrogen phosphate (8·905 g.) and sodium hydroxide (0·33 g.) per l. of solution.

Detection of the Amylosaccharides on Paper.—After ionophoresis of the amylosaccharides the paper was dried (100—110°), neutralised by immersion in water–ethanol–concentrated hydrochloric acid (10 : 1 : 1 by volume) and dried. The location of the amylosaccharides was revealed (1) by spraying the paper lightly with ethanolic iodine (0·4%) and allowing the excess of iodine to volatilise, or (2) by allowing the paper to remain in an atmosphere of iodine vapour for 1 hr. (cf. Greenway *et al.*, *loc. cit.*). The colours so produced tended to fade slowly although in some cases they were still clearly discernible after several months. The colours could be regenerated by the application of either of the above methods. The colours observed are listed in Table 2.

Table 2. *Colours produced by reaction of iodine with some amylosaccharides on paper.*

Amylopectin	Reddish-purple	*N. perflava* polysaccharide	Dark brown
Amylose	Blue	α-Schardinger dextrin	Brown
Glycogens	Yellow-brown	β-Schardinger dextrin	Yellow

Sensitivity of the Method for the Detection of Amylose and Amylopectin.—The ethanolic iodine spray described above was more sensitive for the detection of amylose (limit 0·1 μg.) than for amylopectin (1·0 μg.) on neutral paper without ionophoresis. As the amount of amylose or amylopectin decreased towards the limit of detection the colours produced faded with increasing rapidity. After ionophoresis under standard conditions 0·1 μg. of amylose could still be detected since it was absorbed at the origin and remained in a compact zone. The amylopectin, because of weak absorption during migration, gave a rather diffuse zone at the limits of detection (1·0 μg.). With mixtures of amylose amd amylopectin and ionophoresis under standard conditions 0·3 μg. of amylose could be detected in the presence of 10 μg. of amylopectin, and 2 μg. of amylopectin in the presence of 2·5 μg. of amylose.

Mobilities and M_G Values.—Mobilities and M_G values were determined after ionophoresis under standard conditions. The limits quoted for the mobilities were obtained from the leading and trailing edges of the migrating zones; 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose and methyl

TABLE 3. *Mobilities and M_G values of some amylosaccharides in ionophoresis in borate buffer* (pH 10).

Amylosaccharide	M_G	Mobility ($cm.^2\ V^{-1}\ sec.^{-1}$)	Amylosaccharide	M_G	Mobility ($cm.^2\ V^{-1}\ sec.^{-1}$)
D-Glucose	1·00	$2·26—2·74 \times 10^{-4}$	Glycogen (rabbit liver) ...	0·31	$0·61—0·90 \times 10^{-4}$
Maltose	0·36	$0·81—1·08 \times 10^{-4}$	α-Schardinger dextrin ...	0·14	—
Amylose	0·18	$0·35—0·57 \times 10^{-4}$	β-Schardinger dextrin ...	0·12	—
Amylopectin	0·25	$0·51—0·69 \times 10^{-4}$	Amylose *	—	$3·1 \times 10^{-4}$
			Amylopectin *	—	$3·6 \times 10^{-5}$

* Values quoted by Northcote (*loc. cit.*) for electrophoresis in free solution in 0·05M-borate buffer, pH 9·2, at 0°.

α-D-xylopyranoside were used to determine the extent of the electroendosmotic flow. M_G values were determined as previously described (Foster, *Chem. and Ind.*, 1952, 828); distances were measured from the centres of the migrating zones. Mobilities and M_G values are listed in Table 3.

The authors thank Dr. S. A. Barker, Dr. E. J. Bourne, and Dr. G. A. Gilbert for generous provision of samples, and Professor F. Smith for specimens of various glycogens.

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8. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part II.* Partial Rate Factors for the Acid-catalysed Bromination of Toluene by Hypobromous Acid.*

By P. B. D. DE LA MARE and J. T. HARVEY.

The ratio of isomers produced in the acid-catalysed bromination of toluene by hypobromous acid in aqueous dioxan as solvent has been determined, by the method of isotopic dilution, as: *ortho*-, 70·3%; *meta*-, 2·3%; *para*-, 27·4%; negligible side-chain substitution accompanies the reaction. Under the same conditions, the kinetic form for the bromination both of toluene and of benzene is $-d[BrOH]/dt = k[ArH][BrOH][H^+]$, toluene reacting 36·2 times faster than benzene. These results are discussed in conjunction with those established for other electrophilic substitutions.

RATES of nitration at the various positions in the aromatic nucleus, relative to those for benzene, have been determined for a number of monosubstituted derivatives of benzene. In contrast, there has been little study of other electrophilic substitutions. In the field of halogenations, there are some scattered observations from which estimates of some of the required isomer ratios can be made, particularly for *para*-substitution determined by molecular halogens (cf. de la Mare, *J.*, 1954, 4450). There are, however, no cases, so far as we are aware, in which complete analyses have been carried out under conditions in which the mechanism of halogenation has been determined, and hence no proper estimates of the partial rate factors, *ortho*-, *meta*-, and *para*- to any single substituent are yet available.

The isotope-dilution method is particularly suitable for the determination of these ratios, and can with proper safeguards be used for the estimation of quite small proportions of isomeric products. The present paper describes the use of this method in determining the proportions of isomers produced in the bromination of toluene, with hypobromous acid as source of electrophilic halogen, under catalysis by perchloric acid, in a mixture of dioxan and water at 25°. The conditions were chosen so that it could be established by kinetic methods that the reagent was a positively charged brominating species, either the brominium cation, Br^+, or the hypobromous acidium ion, $BrOH_2^+$.

* Part I, *J.*, 1954, 1290.

Experimental

Materials and Methods.—Dioxan was refluxed with 2N-hydrochloric acid in a stream of nitrogen for 12 hr., and was then partially dried with solid sodium hydroxide. Peroxidic impurities were then removed by shaking with ferrous sulphate. The product was stored over ferrous sulphate in an atmosphere of nitrogen in the dark, and was distilled from sodium hydroxide when required. Toluene (sulphur-free) was fractionated; it had b. p. 110°/758 mm., n_D^{22} 1·4893. Benzene (" AnalaR ") was fractionated and had b. p. 80°/760 mm., n_D^{18} 1·5015. Hypobromous acid was prepared by shaking together bromine, water, and silver phosphate; the product was filtered, distilled under reduced pressure, shaken with carbon tetrachloride, centrifuged, and stored over mercuric oxide at 0°; it was used as soon as possible after preparation. Radioactive hypobromous acid was prepared similarly, irradiated ammonium bromide, supplied by A.E.R.E., Harwell, being introduced into the mixture of bromine and water before addition of the silver phosphate. All measurements of radioactivity were made with the isotope ^{82}Br, after complete decay of the shorter-lived isotope, ^{80}Br. Reference samples of the bromobenzoic acids were prepared by recrystallisation of commercial specimens; they had the following m. p.s: *ortho-*, 146·5°; *meta-*, 155°; *para-*, 251°. Reference samples of the bromotoluenes were prepared similarly, and had the following properties: *ortho-*, f. p. −25·8°; *para-*, f. p. 26·8°. Other reagents were of analytical-reagent quality.

Measurements of radioactivity were made with standard equipment. All counts were corrected for background (usually about 10 counts per min.), and for radioactive decay, as has been described elsewhere (cf. de la Mare, *J.*, 1955, 3196).

Kinetics of Disappearance of Hypobromous Acid.—The reactions were carried out in blackened bottles, and were followed iodometrically. Blank determinations were carried out accompanying each run, to allow a small correction to be made for the decomposition of hypobromous acid in the solvent. The following is an example of a typical kinetic run. From a solution of toluene (0·00799M), hypobromous acid (0·00133M), and perchloric acid (0·00320M), all in 50% dioxan (a mixture of equal volumes of dioxan and water, measured at room temperature), samples (25 ml.) were removed at intervals for titration against 0·00930N-sodium thiosulphate, with starch as indicator. A blank, with toluene omitted, was run side by side with this measurement.

Reaction			Blank		
Time (min.)	Titre (ml.)	10^2k_1 (min.$^{-1}$)	Time (min.)	Titre (ml.)	10^2k_1 (min.$^{-1}$)
0·0	7·17	—	0·0	7·84	—
5·38	5·85	3·78	5·10	7·68	0·40
10·67	4·88	3·61	11·30	7·52	0·37
15·12	4·23	3·49	17·60	7·40	0·33
19·55	3·66	3·44	27·20	7·33	0·25
27·40	2·95	3·24			

The quoted values of k_1, the first-order rate-coefficients for the disappearance of hypobromous acid, have been calculated by using the formula $k_1 = 2{\cdot}303 \log_{10} [a/(a-x)]/t$. They fall through the course of the reaction, partly because the rate is dependent on the concentration of toluene, and also partly because no allowance has yet been made for the rate of spontaneous decomposition of hypobromous acid. Since this reaction is of different kinetic form from the main reaction, the results quoted below are all initial second-order rate-coefficients, obtained in the following way. The initial values of k_1 were obtained by graphical extrapolation, and from these were subtracted the initial rate of decomposition of the blank. The resulting corrected initial first-order rate-coefficients were converted into second-order rate-coefficients by dividing by the concentration of aromatic compound. The latter are given in units l. mole^{-1} min.$^{-1}$, and all refer to a temperature of 25·0°. The following values show the results of varying the concentrations of reactants.

(i) Toluene, 0·0080M; $HClO_4$, 0·0032M:

BrOH (M)	0·0008	0·0013	0·0018	
k_2 (l. mole^{-1} min.$^{-1}$)	4·30	4·46	4·25	

(ii) $HClO_4$, 0·0032M; BrOH, *ca.* 0·0013M:

Toluene (M)	0·0050	0·0080	0·0090	0·0170
k_2 (l. mole^{-1} min.$^{-1}$)	4·50	4·46	4·34	4·35

(iii) BrOH, *ca.* 0·0013M; toluene 0·008—0·015M:

$HClO_4$ (M)	0·0016	0·0032	0·0048	0·0065	0·0081	0·0096
k_2 (l. mole^{-1} min.$^{-1}$)	1·7	4·4	6·4	8·6	10·6	12·3
k_2/H^+ (l.^{2} mole^{-2} min.$^{-1}$)	1060	1380	1330	1320	1310	1280

The results show very clearly that, at 25° in 50% dioxan as solvent, the kinetic form of the reaction is $-d[BrOH]/dt = k[ArH][BrOH][H^+]$. For toluene, the mean value of k is 1300 l.^{2} mole^{-2} min.$^{-1}$. For benzene, the same kinetic form was observed, as is shown by the following results, all under the same conditions of solvent and temperature:

(i) Benzene, 0·014M; $HClO_4$, 0·066M:

BrOH (M)	0·0009	0·00128
k_2 (l. mole^{-1} min.$^{-1}$)	2·44	2·24

(ii) $HClO_4$, 0·066M, BrOH, 0·0013M:

Benzene (M)	0·011	0·014	0·016
k_2 (l. mole^{-1} min.$^{-1}$)	2·39	2·24	2·37

(iii) BrOH, *ca.* 0·0013M; benzene, 0·011—0·016M:

$HClO_4$ (M)	0·027	0·044	0·066	0·088	0·111	0·133	0·141
k_2 (l. mole^{-1} min.$^{-1}$)	0·91	1·52	2·38	3·0	4·2	4·9	5·2
k_2/H^+ (l.^{2} mole^2 min.$^{-1}$)	33·7	34·6	36·4	34·1	37·9	36·8	36·9

From these values, for benzene, k = 35·9 l.^{2} mole^{-2} min.$^{-1}$ in 50% dioxan at 25°.

Proportions of Isomers Formed in the Bromination of Toluene.—(a) para-*Substitution.* Radioactive *p*-bromotoluene was prepared from *p*-toluidine by the Sandmeyer procedure, including with the hydrobromic acid and cuprous bromide *ca.* 3 g. of radioactive ammonium bromide. The product was crystallised several times from ethanol at low temperature, giving a material of m. p. 26·8°.

To a solution (8 l.) of hypobromous acid and perchloric acid (0·0130M) in 50% dioxan was added toluene (27·31 g.). After 6 min., the titre of a 25-ml. aliquot portion of the reaction mixture had fallen from 6·76 ml. of 0·1104N-$Na_2S_2O_3$ to 1·50 ml. In the same time, a blank solution had fallen in titre by 0·20 ml. The reaction was stopped by adding sodium formate and alkali. To 7700 ml., which, from the fall in titre corrected for blank decomposition, should have contained 14·7 g. of mixed bromotoluenes, were added 2·915 g. of radioactive *p*-bromotoluene. The resulting mixture was extracted with ether. The ether-extract was washed with water and fractionated. There were obtained 11 g. (63%) of crude bromotoluenes, b. p. 175—185°/760 mm., f. p. −10·9°. This material was redistilled twice, *ca.* 1 g. of distillate being rejected each time. The product then had f. p. −11·1°, and was crystallised twice from ethanol at low temperature. The product (1 g.) had m. p. 26·8°. The specific activity of this material was compared in ethanol with that of the original radioactive *p*-bromotoluene. The latter (0·00782M) gave a count of 129/min. The former (0·0281M) gave counts which, on interpolation to the same time, had a value of 195 counts/min. Hence the reaction mixture, after addition of radioactive material, contained 6·94 g. of *p*-bromotoluene, of which 4·02 g. (27·4%) had been produced in the reaction.*

(b) ortho-*Substitution.* The procedure was essentially that used for the *para*-isomer. The reaction mixture contained 0·0391M-toluene, 0·0181M-hypobromous acid, and 0·013M-perchloric acid. After reaction for 20 min., 11·63 g. of mixed bromotoluenes had been produced. To the reaction mixture were added 3·973 g. of radioactive *o*-bromotoluene, m. p. −25·9°, which had been prepared from *o*-toluidine. The recovered crude bromotoluenes (10 g.) were oxidised by 36 hours' refluxing with aqueous potassium permanganate. There were recovered 4 g. of bromobenzoic acids, m. p. 138°; these were recrystallised many times from water, with rejection of early fractions which consisted largely of *p*-bromobenzoic acid. There were finally obtained 1·3 g., m. p. 146·5°, unchanged in m. p. or in specific activity by further recrystallisation. The specific activity was determined in ethanol, and was compared with that of the original *o*-bromotoluene, and with that of a specimen of *o*-bromobenzoic acid, m. p. 146·5°, prepared from the latter by a similar oxidation. The values obtained were respectively, for a 0·382M-solution, 84·1, 254, and 260 counts/min. By using the mean specific activities of the two reference materials for calculation of the degree of dilution, it follows that 70·2% of *o*-bromotoluene was produced.

(c) meta-*Substitution.* It would be impracticable to use the above method for determining the % of *meta*-substitution, since the degree of dilution of the active sample would be too high. Instead, the reaction was carried out by using radioactive hypobromous acid. The reaction mixture contained initially 0·0516M-toluene, 0·00261M-hypobromous acid, and 0·013M-perchloric acid. After 20 min., its decrease in titre showed that 0·4554 g. of mixed bromotoluenes had been produced. The reaction was stopped, and to the mixture were added 9·67 g. of inactive *m*-bromotoluene. The crude mixture of bromotoluenes, isolated in the usual way, was oxidised

* The f. p. of the crude bromotoluenes, in conjunction with the data of Van der Laan (*Rec. Trav. chim.*, 1907, **26**, 297) gives a value of 29·3%.

as described above. The resulting mixture of bromobenzoic acids was purified by fractional crystallisation, giving 1·5 g. of *m*-bromobenzoic acid, m. p. and mixed m. p. 155°. This material was still contaminated with traces of isomers of high specific activity. Successive crystallisations gave specific activities, expressed in counts/min. of an alkaline solution of 0·1603 g. in 15·0 ml. (0·0532M), of 168, 157, 150, 127, and 125. The limiting specific activity, on comparison with that of the original hypobromous acid, which had been converted into bromide ion for counting and had an activity of 708 counts/min. for a 0·000320N-solution, corresponds with the formation of 2·3% of *m*-bromotoluene.

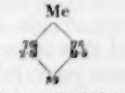
(d) *Side-chain substitution.* In the crude mixture of bromotoluenes isolated in one of the above reactions, benzyl bromide was estimated gravimetrically as silver bromide. There appeared to be produced in the bromination less than 0·01% of the product of side-chain substitution.

Discussion

All the values given above are entirely independent; their sum, 99·9%, accounts for all the measured reaction within experimental error, and this is a partial check on the reliability of the values given. For the purposes of discussion, the following rounded-off values are adopted: *ortho*-, 70·3%; *meta*-, 2·3%; *para*-, 27·4%; side-chain, 0·0%.

The fact that side-chain substitution is nearly absent makes it certain that toluene is brominated in this reaction by an electrophilic process rather than by one involving bromine atoms. The kinetic form makes it clear that, as in investigations by other workers in similar conditions (Derbyshire and Waters, *J.*, 1950, 564; Shilov and Kaniaev, *Compt. rend. Acad. Sci. U.S.S.R.*, 1939, **24**, 890; Branch and Brynmor Jones, *J.*, 1954, 2317), the reagent is either Br^+ or $BrOH_2^+$.

Combination of the relative rates of reaction of benzene and toluene with the above isomeric proportions gives the following values for the partial rate factors in the bromination of toluene. For comparison are given also values for nitration (Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291), and, incompletely, for bromination by molecular bromine (Robertson, de la Mare, and Swedlund, *J.*, 1953, 782).



Br^+ or $BrOH_2^+$
(I)

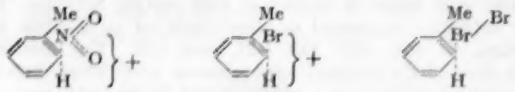
NO_2^+
(II)

Br_2
(III)

The similarity between the results obtained for bromination with positive bromine and those available for nitration by the nitronium ion is remarkable. In both cases, the *meta*-position is activated by only a small factor, whereas the *para*-position is considerably more activated. Examination of the values for *ortho*-substitution suggests that there is somewhat more resistance to entry of the nitro- than to that of the bromo-group *ortho* to a methyl substituent. It is often considered (cf. Holleman, *Chem. Rev.*, 1925, **1**, 187) that steric hindrance is in general greater for *ortho*-bromination than for *ortho*-nitration; but this is a conclusion reached by consideration of data for molecular bromination as compared with ionic nitration. When both reactions are carried out with positively charged reagents, a different situation appears to arise, as shown by the present comparison.

That steric hindrance should be greater for *ortho*-nitration than for *ortho*-bromination is not unreasonable if consideration is given to the most probable geometry of the transition state for nitration. The nitronium ion is linear, but, in reacting as an electrophilic reagent, its shape must be distorted towards that of the nitro-group. Its final most stable conformation is coplanar with the aromatic ring; and during the course of the reaction, while both the entering and the leaving group are still bound to the ring, repulsions involving the leaving hydrogen atom must not become too large. It follows that, as the nitro-group approaches the aromatic ring and displaces the proton downwards, so that the attacked carbon atom approaches the tetrahedral configuration (a type of transition state favoured by most writers on aromatic substitution; cf. Hughes, Ingold, and their co-workers, *J.*, 1937, 1257; 1941, 608), the nitro-group will tend to maintain itself so that its oxygen

atoms lie parallel with the aromatic ring, as is indicated in formula (IV), the hydrogen atom lying below the entering group :



(IV) (V) (VI)

The effective radius of the nitro-group in the direction of the flanking *ortho*-methyl group is likely, therefore, to be greater than that of the spherical bromine substituent (formula V).

It seems, therefore, that the intrinsic reactivity of the position *ortho* to a methyl group is larger than that of the corresponding *para*-position. This is attributed essentially to the inductive influence of the substituent. Electrons are made available inductively more readily by electron-releasing substituents at the *ortho*- than at the *para*-position. In this connection there is no means of distinguishing between the inductive effect working through the bonding system and the same effect working directly through space; but analogy with the apparently greater selectivity of the *para*- than of the *ortho*-position for the acceptance of electrons by conjugative relay (cf. Waters, *J.*, 1948, **727**; Hughes and Ingold, *J.*, 1941, **608**; Bradfield, *Trans. Faraday Soc.*, 1941, **37**, 746) makes us think that the direct effect may be of some importance in these reactions.

The partial rate-factor for the bromination of toluene in the *para*-position, with molecular bromine as reagent, is 1990 (Robertson, de la Mare, and Swedlund, *loc. cit.*; de la Mare, *J.*, 1954, **4450**). With this reagent, *para*-substitution predominates, accounting for 69% of the product. The contrast in proportion of *para*-substitution between molecular and ionic bromination might at first sight be considered to involve only differential steric hindrance, Br_2 being larger than Br^+. Consideration of models (cf. formula VI) suggests, however, that the eliminated bromide ion, coming from a bromine molecule, is unlikely to be in a situation where it would greatly be interfered with by an *ortho*-methyl group. It is considered probable, therefore, that the larger amount of *para*-substitution, found when molecular bromine is the reagent, is partly a reflection also of the relatively greater importance of conjugative electron-release with these molecular reagents.

De la Mare and Robertson (*J.*, 1948, **100**) have proposed that inductive, as compared with electromeric, effects of substituents are called out more powerfully in electrophilic substitutions determined by formally positive than by comparable formally neutral reagents. This theory was developed from consideration of certain differences between nitration by the nitronium ion and halogenation by halogen molecules. A second factor requires consideration in regard to the latter reaction, namely, that the halogen molecule appears to be particularly effective in evoking electromeric electron release, and a theoretical interpretation of this fact has been given elsewhere (*J.*, 1949, 2871).

The present investigation represents a stage in an experimental approach towards a test of the theory by comparing reagents which, though of different charge-type, introduce the same group into the aromatic nucleus. The results, as indicated for example in comparisons between (I) and (III), are consistent with the theory outlined. Berliner and Berliner (*J. Amer. Chem. Soc.*, 1954, **76**, 6179) have, on the basis of independent experiments, reached similar theoretical conclusions. H. C. Brown and Nelson (*ibid.*, 1953, **75**, 6292) appear to take a similar view concerning the relatively greater importance of conjugative influences in halogenation than in nitration. It is surprising, therefore, that H. C. Brown and McGary (*ibid.*, 1955, **77**, 2310) should have so misunderstood the paper by Robertson, de la Mare, and Swedlund (*loc. cit.*) as to state that the latter authors regard as anomalous those differences, which they discuss, between these reactions. The theory set forth by the latter authors was regarded by them, and is regarded by the present writers, as being in accordance with the experimental results so far ascertained.

We are indebted to Professor C. K. Ingold, F.R.S., and to Professor E. D. Hughes, F.R.S., for many fruitful discussions. Preliminary measurements relating to the kinetics of the reactions herein studied were made by Dr. A. D. Ketley.

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9. *The Reaction between* tert.*-Butyl Chloride and Sodium Thiophenoxide.*

By P. B. D. de la Mare and C. A. Vernon.

The reaction between *tert.*-butyl chloride and sodium thiophenoxide is kinetically of the second order, and results in the formation of *ca.* 90% of olefin and a small amount of *tert.*-butyl phenyl sulphide. This product is stable under the conditions of the measurements. The main reaction is considered to be a bimolecular elimination (*E*2), and is more rapid than the corresponding reaction between *tert.*-butyl chloride and either sodium phenoxide or sodium ethoxide. The theoretical significance of these results is discussed.

Sodium thiophenoxide is, in ordinary circumstances, more reactive by factors between 100 and 1000, and therefore has greater nucleophilic power, than either sodium ethoxide or sodium phenoxide in nucleophilic displacements at a carbon centre (for rate comparisons, cf. Quayle and Royals, *J. Amer. Chem. Soc.*, 1942, **64**, 226; de la Mare and Vernon, *J.*, 1952, 3331). On the other hand, the thiophenoxide ion is less basic than either the ethoxide or the phenoxide ion, if this property is measured by the degree of dissociation of the conjugate acid (thiophenol, $pK_a = 9{\cdot}3$ in 95% ethanol, Schwartzenbach and Rudin, *Helv. Chim. Acta*, 1939, **22**, 1360; phenol, $pK_a = 12{\cdot}8$ in 95% ethanol, *idem, ibid.*; ethanol, $pK_{auto} = 19{\cdot}0$; see Remick "Electronic Interpretations of Organic Chemistry," Wiley and Sons, New York, 1949, p. 251). The nucleophilic powers of anions, as judged from their rates of attack on a carbon centre, do not bear a direct relationship to their basic strengths, as judged from their equilibrium properties in combination with hydrogen (cf. Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273; Hughes, *Quart. Rev.*, 1951, **5**, 245; Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 331).

A better correlation would be expected between basic strength and rate of attack upon hydrogen. If an alkyl halide were chosen for which, with ethoxide ions, much bimolecular elimination accompanies substitution, a much smaller proportion of elimination should occur in its reaction with thiophenoxide ions. Ethylene dibromide exemplifies this behaviour (Hine and Brader, *J. Amer. Chem. Soc.*, 1953, **75**, 3964).

It is of interest to compare directly the effect of different anions on the rates of elimination from an organic halide. In another connection we were examining the reaction of *tert.*-butyl chloride with sodium thiophenoxide; Ipatieff, Pines, and Friedman (*J. Amer. Chem. Soc.*, 1938, **60**, 2731) found only chloride ions and unchanged thiophenol as products of this reaction. Re-examination has confirmed that the main process involves elimination, but a small proportion of the product of substitution can be isolated.

Experimental

Product Analysis.—*tert.*-Butyl chloride (28 g.; b. p. 51°/760 mm.) was refluxed with 1·7N-sodium thiophenoxide in ethanol (200 ml.). The volatile olefinic product (12·6 g.) was collected in a cold trap, and was then allowed to evaporate into carbon tetrachloride (250 ml.) containing bromine (60 g.). Reaction was very rapid. The excess of bromine was removed and the organic material was dried and fractionated, giving, after removal of the solvent, (*a*) 11·9 g., b. p. 150—155°/765 mm., n_D^{25} 1·5080, (*b*) 1·0 g., b. p. 155—160°, n_D^{25} 1·5098; (*c*) 2 g. of residue of high b. p. Refractionation of (*a*) gave a main fraction, b. p. 148—150°/763 mm., n_D^{25} 1·5068 (Found: C, 22·4; H, 3·8. Calc. for $C_4H_8Br_2$: C, 22·2; H, 3·7%). Suter and Zook (*J. Amer. Chem. Soc.*, 1944, **66**, 738) record, for 1 : 2-dibromo-2-methylpropane, n_D^{25} 1·5070.

The alcoholic reaction mixture was added to 2N-sodium hydroxide (500 ml.) and extracted with ether. The extract was washed with alkali and water, dried, and fractionated, giving 1·0 g., b. p. 90—92°/15 mm., n_D^{25} 1·5307, f. p. −13° (Found: C, 72·3; H, 8·9; S, 18·7. Calc. for $C_{10}H_{14}S$: C, 72·3; H, 8·4; S, 19·3%). The properties of this material accord with those recorded by Ipatieff, Pines, and Friedman (*loc. cit.*) for *tert.*-butyl phenyl sulphide, b. p. 73°/5 mm., n_D^{20} 1·5335.

Kinetic Experiments.—The following are details of an experiment in which the reaction of *tert.*-butyl chloride with sodium thiophenoxide in ethanol at 44·6° (5·53 ml. portions, in sealed

tubes) was followed (*a*) by titration in ethanol with standard acid, lacmoid being used as indicator, in order to measure the total rate of production of hydrogen chloride; and (*b*) by titration in slightly aqueous ethanol with sodium hydroxide, phenolphthalein being used as indicator, in order to measure the rate of production of thiophenol which, under these conditions, is titrated as a weak acid.

Time (min.)	0·0	19·0	43·5	115	199	259	408	∞
Titre (ml. of 0·0878N-HCl; lacmoid)	45·68	44·90	44·00	41·85	39·70	38·20	35·60	25·60
Titre (ml. of 0·0878N-NaOH; phenolphthalein)	0·26	—	—	3·90	—	—	9·41	19·04
10^3k_2 (l. mole^{-1} min.$^{-1}$)	—	2·75	2·73	2·57	2·55	2·65	2·62	—
Elimination (%)	—	—	—	95	—	—	91	93·5

From values obtained similarly at 58·4° (k_2 = 0·0130 l. mole^{-1} min.$^{-1}$) and at 68·0° (k_2 = 0·0388 l. mole^{-1} min.$^{-1}$) at both of which temperatures there was also found at the end of the reaction 93% of elimination, it can be calculated that the Arrhenius parameters of the reaction are E = 24·8 kcal. mole^{-1}, and $\log_{10} B$ = 14·46 l. mole^{-1} min.$^{-1}$.

The following mean rate coefficients show the dependence of rate upon salt concentration:

$[SPh^-]$ = 0·23, k_2 = 0·00312; $[SPh^-]$ = 0·70, k_2 = 0·00264 l. mole^{-1} min.$^{-1}$.

The values illustrate that the reaction is of the second order; the customary "dilution effect" results in a small increase in the rate coefficient when the concentration is decreased.

The following experiment was designed to test the stability of *tert.*-butyl phenyl sulphide. Samples (5·0 ml.) of *tert.*-butyl phenyl sulphide (0·0766M, in 0·432M-sodium ethoxide) were heated at 89·6°, and were titrated at intervals with 0·0948N-acid (phenolphthalein) with the following results:

Time (min.)	0·0	4·20	1680	3870	∞ (calc.)
Titre (ml. of 0·0948N-HCl)	22·80	22·60	22·50	22·25	18·76

Since thiophenol is titrated as a weak acid under these conditions, the calculated infinity titre is that expected for complete formation either of *tert.*-butyl ethyl ether, by reaction (i), or of thiophenol, by reaction (ii):

$$Bu^tSPh + OEt^- \longrightarrow Bu^tOEt + SPh^- \quad . . . . . \quad (i)$$

$$Bu^tSPh + OEt^- \longrightarrow EtOH + CH_2{:}CMe_2 + SPh^- \quad . . . . . \quad (ii)$$

That *tert.*-butyl phenyl sulphide would survive, even under conditions much more drastic than those of the kinetic measurements, is shown by the small change in titre in the above experiment.

The following result shows that added *tert.*-butyl phenyl sulphide does not significantly affect the rate of solvolysis of *tert.*-butyl chloride. Samples (5 ml.) were removed from a solution containing *tert.*-butyl chloride (0·078N) and *tert.*-butyl phenyl sulphide (0·033M) in ethanol at 43·9°, and were titrated with 0·0217N-alkali, with lacmoid as indicator except where otherwise stated:

Time (min.)	0·0	1138	1150	1673	2788	5963	7118	7133	∞
Titre (ml.)	0·15	1·88	1·89 *	2·58	3·95	7·30	8·30	8·42 *	18·10
10^5k_1 (min.$^{-1}$)	—	8·5	8·2	8·7	8·5	8·5	8·5	8·5	—

* Titrated in pre-neutralised slightly aqueous ethanol with phenolphthalein as indicator.

The mean rate-coefficient (8·5 × 10^{-5} min.$^{-1}$) is only slightly greater than the corresponding value (8·0 × 10^{-5} min.$^{-1}$ at 44·6°; see also Grunwald and Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 849) obtained in the absence of *tert.*-butyl phenyl sulphide. Furthermore, the *tert.*-butyl phenyl sulphide is not converted into thiophenol in the course of the reaction, since the titrations with phenolphthalein as indicator agree with those obtained by using lacmoid. In the presence of 0·10M-thiophenol, the solvolysis at 44·6° was found to have a velocity coefficient k_1 = 9·2 × 10^{-5} min.$^{-1}$, being thus insignificantly catalysed by added thiophenol. These small alterations in rate, observed when thiophenol or *tert.*-butyl phenyl sulphide are added, should probably be regarded as co-solvent effects.

In the presence of phenol, in amount equivalent to the alkali, the nucleophilic reagent is substantially the phenoxide ion, the equilibrium $OEt^- + PhOH \rightleftharpoons OPh^- + EtOH$ lying largely to the right-hand side. A solution thus prepared of sodium phenoxide (0·50M) reacts with *tert.*-butyl chloride (0·19M) with an initial first-order rate-coefficient at 43·7° of 2·6 × 10^{-4} min.$^{-1}$, substantially constant over 70% of the reaction. The rate of reaction is therefore significantly increased by change of the reagent from ethanol to phenoxide ions. The

products of this reaction have been shown by Lewis (*J.*, 1903, 329) to include 2-methylpropene and, as a main product of substitution, *p-tert.*-butylphenol, which no doubt is the result of production, in the unimolecular component of the reaction, of the *tert.*-butyl carbonium ion, which can then react with the phenoxide ion to give nuclear substitution (cf. Gelles, Hughes, and Ingold, *J.*, 1954, 2198).

The formal initial second-order rate-coefficient, corrected for the concomitant solvolysis, is, for the reaction of *tert.*-butyl chloride with 0·50M-phenoxide ions at 43·7°, $0{\cdot}33 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$. The rate of solvolysis is similarly accelerated ($k_2 = 0{\cdot}26 \times 10^{-3}$ l. mole^{-1} min.$^{-1}$ at 43·7°) by the addition of 0·54M-sodium ethoxide. These values are, however, subject to uncertainty in the rate of solvolysis in the presence of the added base.

Discussion

The elimination of hydrogen chloride from *tert.*-butyl chloride under the influence of sodium thiophenoxide appears to be considerably more rapid (by a factor of about a power of ten) than the corresponding reactions involving either sodium phenoxide or sodium ethoxide. This result is at first sight surprising, in view of the relatively weak basic properties of the thiophenoxide ion. Other possibilities for the reaction process therefore require careful scrutiny. It appears theoretically possible that the reaction might in fact be a substitution, followed by decomposition of the product, *tert.*-butyl phenyl sulphide.

$$Bu^tCl + SPh^- \longrightarrow Bu^tSPh + Cl^- \quad . . . . . (1)$$

$$Bu^tSPh \longrightarrow Me_2C{:}CH_2 + H^+ + SPh^- \quad . . . . . (2a)$$

$$\downarrow Bu^tCl$$

$$Bu^t_2SPh^+\}Cl^- \longrightarrow 2Me_2C{:}CH_2 + 2H^+ + SPh^- + Cl^- \quad . . . . (2b)$$

Route (2*a*) has been excluded experimentally; for *tert.*-butyl phenyl sulphide has been shown to be stable under the conditions of the measurements. Route (2*b*) is also excluded, for the following reasons. The sulphonium salt $Bu^t_2SPh^+\}Cl^-$ does not accumulate during the course of the reaction, as has been shown by the fact that the development of thiophenol parallels the formation of total acid. Hence, if the sulphonium salt is formed at all, it must be formed and decomposed more rapidly than the overall measured rate of reaction between *tert.*-butyl chloride and thiophenoxide ions. Separate experiments showed, however, that *tert.*-butyl phenyl sulphide is stable in the presence of *tert.*-butyl chloride, and does not appreciably influence the rate of solvolysis of the latter compound.

Since the observed kinetic form [equation (3)] can be rewritten as in equation (4), the possibility should be considered that the elimination is actually a ternary reaction between *tert.*-butyl chloride, ethoxide ions, and thiophenol. From the dissociation

$$d[HCl]/dt = k[Bu^tCl][SPh^-] \quad . . . . . (3)$$

$$d[HCl]/dt = k[Bu^tCl][OEt^-][PhSH]/[EtOH] \quad . . . . . (4)$$

constants of ethanol and thiophenol, however, it can be calculated that the concentrations of ethoxide ions and of thiophenol under the conditions of the reaction are each less than about 10^{-4}M. The adoption of such a view of the reaction would entail the corollary that 10^{-4}M-ethoxide ions in conjunction with 10^{-4}M-thiophenol is a better combination for elimination than M-ethoxide ion in conjunction with *ca.* 17M-ethanol. In other words, one would have to conclude that thiophenol, as compared with ethanol, catalyses electrophilically the removal of hydrogen chloride under the influence of sodium ethoxide by a factor of the order of 10^{10}. This seems to us to be especially unlikely, and we prefer the view that the reaction of *tert.*-butyl chloride with sodium thiophenoxide is indeed a bimolecular elimination (*E*2).

It is well known that nucleophilic power as measured by rate of attack on carbon is not well correlated with basicity. Anions of the type RS^- (R = H, alkyl, or aryl) appear to give the most striking examples of this type of deviation from simple theory, and the phenomenon seems to be associated with descent of the Periodic Table, since it appears also in the comparisons (cf. de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3200)

between basicity and power of nucleophilic attack in the reaction of halide ions with alkyl halides. It seems possible that it is connected, in some way not yet fully understood, with the greater polarisability of elements of the higher periodic groups.

There are very few examples, as far as we are aware, of comparisons of rates of nucleophilic attack on hydrogen which include ions of the type RS^-. Hine's case (*J. Amer. Chem. Soc.*, 1950, **72**, 2438) of the reaction between anions and chloroform involves, according to his preferred mechanism, a pre-equilibrium (5).

$$CHCl_3 + B^- \rightleftharpoons CCl_3^- + BH^+ \text{ (fast)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$CCl_3^- \longrightarrow CCl_2 + Cl^- \text{ (slow)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$CCl_2 \longrightarrow \text{products (fast)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The measured rate-coefficients, in this case, should therefore be proportional to the equilibrium constant for the first reaction (5) and would, by analogy with the situation in the equilibrium (8) be greater for $B = OH^-$ than for $B = SH^-$,

$$H_3O^+ + B^- \longrightarrow H_2O + BH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

independently of the relative rates of attainment of equilibrium.

We do not yet know whether an abnormally great reactivity of the thiophenoxide ion is a characteristic of synchronous reactions involving displacement of a nucleophilic group, as seems possible, or more generally of rate processes involving attack on covalently bound atoms, including hydrogen. But the present example serves to illustrate once again the difficulties involved in attempting to correlate, over a wide range of structural differences, the rates of reaction with equilibria.

We are indebted to Professors E. D. Hughes, F.R.S., and C. K. Ingold, F.R.S., for their interest.

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10. *The Enzymic Synthesis and Degradation of Starch. Part XX.* The Disproportionating Enzyme (D-Enzyme) of the Potato.*

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It is shown that D-enzyme (*Nature*, 1953, **172**, 158) is different from phosphorylase, R-enzyme, and the amylases. It has not yet been possible to separate D-enzyme from Q-enzyme but it is demonstrated that the branching and the disproportionating activity are due to independent enzymes.

Evidence is presented which shows that D-enzyme is a transglycosylase, transferring two or more glucose units from a maltodextrin substrate to a suitable acceptor and that, in the transfer, only α-1 : 4-glucosidic links are synthesised.

The natural substrates for D-enzyme appear to be the maltodextrins, from maltotriose upwards; neither glucose nor, in all probability, maltose functions as donor substrate. The enzyme is not so selective with respect to the "accepting" molecule.

The anomalous position of maltose in this system is discussed.

IT has been shown (Part XVIII, *J.*, 1953, 1422) that Q-enzyme cannot effect branching of short amylose-type chains, the minimum chain length for rapid action being about 40 glucose units. In a further investigation of potato Q-enzyme we examined the effects of this enzyme preparation on the lower range of maltodextrins, *viz.*, on malto-triose, -tetraose, and -pentaose. In each case, products were synthesised which were stained brown-red by iodine (the substrates are achroic) and paper chromatograms of the digests revealed that

* Part XIX, *J.*, 1954, 4440.

sugars, including glucose, having R_F values higher and lower than that of the substrate had also been formed. Reference will be made later to the striking observation that maltose, the first member of the maltodextrin series, appears not to function as a substrate in this reaction. The iodine-staining products proved to be higher maltodextrins, *i.e.*, to consist of chains of α-1 : 4-linked glucose units only, as they were completely degraded by β-amylase. On β-amylolysis, the Q-enzyme digests became achroic and then contained only three sugars, identified by R_F values as glucose, maltose, and maltotriose. The same observations were made with crude potato juice as the enzyme source, although chromatographic analysis was complicated in this case by the presence of glucose, fructose, and sucrose in the juice.

It was clear that the enzyme system of the potato was capable of disproportionating short-chain linear dextrins into products of lower and higher molecular weight and it became necessary to determine whether this action was due to one of the known starch-metabolising enzymes, *i.e.*, phosphorylase, Q-enzyme, or R-enzyme, or to a hitherto undetected enzyme.

Non-identity of the Disproportionating Factor with Known Enzymes.—The Q-enzyme preparation used contained phosphorylase in small amount and, if a trace of mineral phosphate were also present, the phosphorylase would catalyse reversible degradation of the maltodextrin and formation of glucose 1-phosphate. Because the affinity of the enzyme for maltodextrins increases with the chain-length of the latter, the tendency in the presence of a limited amount of the Cori ester would be towards the synthesis of longer maltodextrin chains. Accordingly, amounts of the Q-enzyme preparation and of a potato phosphorylase equal with respect to phosphorylase activity were separately incubated with maltopentaose and the formation of iodine-staining material was measured. The results (Table 1) showed that the Q-preparation was much more efficient in synthesis than was the phosphorylase, whether or not mineral phosphate was added to the digests. It followed that the synthesis of iodine-staining dextrins by the Q-preparation cannot be ascribed entirely to the phosphorylase which it contains.

A fractionation of potato juice designed to lead to maximum recovery of Q-enzyme led also to maximum recovery of disproportionating activity. Inhibitors also failed to distinguish between the two types of activities : in experiments under the usual conditions (Bailey, Thomas, and Whelan, *Biochem. J.*, 1951, **49**, lvi) mercuric chloride caused roughly equal inhibition of both, and ammonium molybdate had no effect on either. It should be noted that R-enzyme is inhibited by molybdate (Part XVIII, *loc. cit.*) and consequently cannot be identical with the disproportionating enzyme. Despite the difficulty experienced in separating the branching (Q-)activity from the disproportionating (D)-activity evidence was obtained that two independent enzymes were involved. The temperature and pH optima of the two activities were determined on the same Q-preparation, the D-activity by measurement of the development of iodine-staining dextrins from maltopentaose and the Q-activity by the diminution in iodine-staining power of amylose. These measurements clearly distinguish between the two activities (see Figs. 1 and 2) and permit the inference that the disproportionating activity of potato juice is probably due to a hitherto undetected enzyme, for which provisionally the name, D-enzyme, is suggested.

Finally, it should be mentioned that the Q-preparation was virtually free from α- and β-amylase. Thus in a period of action (on maltotetraose) during which the absorption value (A.V.; see *J.*, 1945, 924 for definition) attained a maximum value, the reducing power increased by only 1·3% of its initial value, a clear indication of the absence of hydrolysis. Moreover, the failure to detect maltose in quantity in the digests also indicates the absence of the amylases.

Action of D-Enzyme on Glucose and the Maltodextrins.—Since experiments designed to remove or inhibit Q-enzyme preferentially had failed, the investigations were pursued with the potato preparation of maximum D-activity which, as mentioned above, was also richest in Q-activity. It will be shown later that the Q-enzyme present in this preparation exerts no branching action during the disproportionation.

The action of D-enzyme on glucose and the maltodextrins was investigated by paper chromatography of the digests. There was no effect with glucose as substrate. With

maltose, small amounts of sugar having the R_F value of glucose were detected after 6 hours; in one experiment only, the chromatograms showed the presence of a saccharide having a R_F value slightly higher than that of maltose. Maltotriose was rapidly disproportionated, the products, named in relation to the observed R_F values, were maltopentaose, glucose (both showing strongly after 0·5 hr.), and a small amount of maltotetraose; thereafter, up to the final observations at 21 hours, all these products increased in amount and spots of lower and zero R_F values appeared. Only a trace of maltose was formed, and this only in the last stage of the reaction. Similar observations were made with maltotetraose and maltopentaose as substrates, glucose and a continuous series of maltodextrins of increasing molecular weight from maltotriose upwards being produced. Maltose constitutes a notable exception, only traces being formed.

The Mode of Action of D-Enzyme.—The simplest explanation of these phenomena is that the potato contains a transglycosylase (D-enzyme) which effects the transfer of glucose units either singly or severally from one maltodextrin substrate (the donor) to another

FIG. 1. *Temperature optima of D- and Q-enzymes at* pH 6·7. *D-Enzyme acting on maltohexaose* (○); *Q-enzyme acting on amylose* (●).

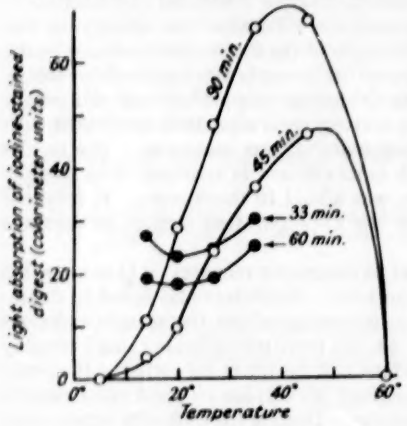
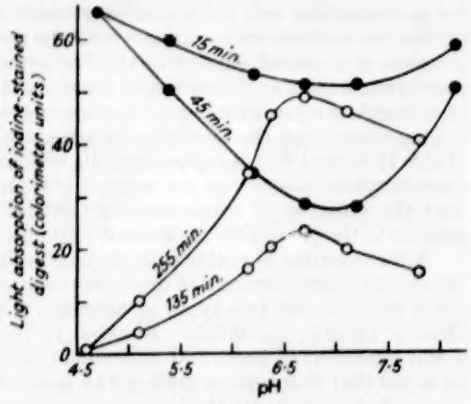


FIG. 2. pH *optima of D- and Q-enzymes at* 15°. *D-Enzyme acting on maltohexaose* (○); *Q-enzyme acting on amylose* (●).



(the acceptor). The indication that only α-1 : 4-links are synthesised in this transfer was strengthened on studying amylolysis of the products of the action of D-enzyme on maltodextrins. (*a*) Maltotetraose was treated successively with D-enzyme and salivary α-amylase and the products were fractionated on a charcoal–Celite column. Three sugars were isolated and identified by chromatographic behaviour on paper as glucose, maltose, and maltotriose, in a combined yield equivalent to 97%. These three sugars, and these alone, are to be expected as products of the α-amylolysis of mixtures of glucose and linear maltodextrins (Whelan and Roberts, *J.*, 1953, 1298). (*b*) It is known that the crystalline β-amylase of sweet potato rapidly degrades maltotetraose and higher maltodextrins but hydrolyses maltotriose only very slowly to give glucose and maltose (Whelan, Bailey, and Roberts, *J.*, 1953, 1293). Chromatographic comparison of the action of β-amylase on maltotriose with that of a mixture of D-enzyme and β-amylase revealed that, whereas β-amylase alone had a barely perceptible effect even after 17 hours, the mixture of enzymes had in 4 hours completely converted the maltotriose into maltose and glucose. This is explicable if D-enzyme converts maltotriose into a mixture of glucose and maltodextrins higher in the series than maltotriose; β-amylase rapidly hydrolyses the higher dextrins to maltose and maltotriose (Whelan and Roberts, *Biochem. J.*, 1954, 58), the latter product acting as further substrate for D-enzyme. The net result of the simultaneous action of D-enzyme and β-amylase is the quantitative conversion of maltotriose into maltose and glucose, as was found.

In another context this experiment is of value inasmuch as it suggests that the slow action of a crystalline β-amylase preparation on maltotriose could be due to its containing a trace of D-enzyme and that enzymically pure β-amylase does not attack maltotriose.

The ultimate result of the action of D-enzyme on a maltodextrin is the establishment of an equilibrated mixture of maltodextrins (excluding maltose) and glucose. Thus, when maltohexaose was digested with D-enzyme, iodine-staining products were formed and the A.V. of the digest rose to a value which remained constant during the period of the experiment (18 hours; see Fig. 3). This experiment incidentally confirms the views that D-enzyme is not a hydrolytic enzyme and that the D-preparation used did not contain α- or β-amylase. Further, it shows that the average chain length of the maltodextrin products of D-enzyme action varies directly with the initial concentration of the maltohexaose substrate since the addition of more maltohexaose to a digest in thich the A.V. had reached a constant value caused a further increase in intensity of staining. It also follows that the apparent cessation of action is not due to inactivation of the enzyme.

The Rôle of Glucose.—There were indications that, in the transglycosylation, glucose cannot act as a donor (*i.e.*, is not itself " transferred " by the enzyme to an acceptor) but can " accept " glycosyl radicals, and it is to be expected therefore that its addition to an equilibrated digest would, as a result of transfer to the added glucose, diminish the average

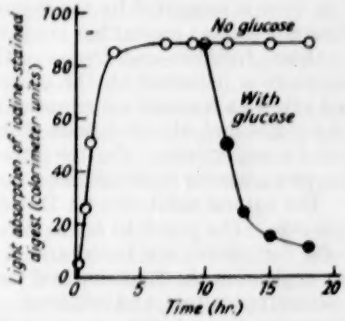


FIG. 3. *The effect of glucose on the equilibrated system D-enzyme + maltohexaose. The digest was divided at 10 hr. and glucose added to one portion. Incubation was at 20°.*

chain-length of the maltodextrins present. This inference was confirmed by experiment. When glucose was added to a digest of maltohexaose by D-enzyme which had attained equilibrium, the digest became achroic (Fig. 3). Paper-chromatographic comparison with a portion of the digest to which glucose had not been added revealed that the glucose-treated digest contained a much higher proportion of dextrins of low degree of polymerisation (DP). It was established that some of the added glucose was incorporated into the maltodextrins formed, by a repetition of this experiment with uniformly labelled [^{14}C]-glucose. Determination of the radioactivity associated with the sugar spots on a paper chromatogram showed each of the dextrins to be appreciably radioactive. A control experiment demonstrated that a non-enzymic exchange of radioactivity had not occurred.

Since the addition of glucose caused a fall in the average degree of polymerisation of the maltodextrins at equilibrium, it was to be expected that the removal of glucose from the equilibrated digest would have the reverse effect and increase the average chain length. Attempts to remove glucose with notatin failed owing to the presence of amylases in the two available specimens of glucose oxidase, but experimental confirmation was obtained in another way. Maltohexaose was incubated with D-enzyme, glucose and other products of low molecular weight were removed by dialysis, and the non-dialysable maltodextrins were isolated. This dextrin mixture was stained red by iodine, did not migrate on a paper chromatogram, and yielded maltose and maltotriose only when treated with β-amylase. Measurements of reducing power showed its average chain length to be 12 units. When this synthetic 12-unit dextrin was again digested with D-enzyme, the iodine stain doubled

in intensity and changed from red to purple, indicating the formation of yet longer-chain dextrins. It is to be remembered that our D-enzyme preparation is in fact a purified Q-enzyme fraction of potato juice, and in the experiment just described there was a suggestion that the Q-enzyme might have exerted some branching action on the 12-unit dextrin, inasmuch as a constant maximum A.V. was not maintained. This matter can be decided only when a D-enzyme free from Q-enzyme has been prepared and studies are proceeding with this object in view.

Glucose added to a digest of the synthetic 12-unit dextrin by D-enzyme had its usual A.V.-lowering effect and the digest became achroic. A comparison was made with the effect of D-enzyme on amylopectin, the outer chains of which average 12 glucose units in length. D-Enzyme lowered the A.V. of amylopectin even before glucose was added, but glucose addition markedly accelerated the rate of fall of A.V. This action on amylopectin could not have been due to the debranching action of R-enzyme contained in the D(Q)-preparation since the effect persisted in the presence of molybdate (cf. Part XIV, *J.*, 1951, 1451; Part XIX, *J.*, 1954, 4440). It may be that the fall of A.V. observed before the addition of glucose was due to further branching of the outer chains of amylopectin by Q-enzyme, but the acceleration of the fall of A.V. by glucose addition rather suggests that it is the D-enzyme which is responsible for the phenomenon and that when glucose is present it acts as acceptor for fragments of the outer chains of amylopectin transferred by D-enzyme. This view is supported by the observation that maltotriose was formed from amylopectin when glucose was present but not in its absence.

Other Acceptors and Donors.—That saccharides other than glucose can function as acceptors is indicated by the observation that methyl α-D-glucoside, maltose, mannose, and xylose each caused a diminution in the A.V. of a digest of maltopentaose with D-enzyme (at equilibrium), the efficiencies of these sugars relative to glucose (=100) being 44, 20, 17, and 15 respectively. On the other hand, fructose, sucrose, and αα-trehalose are not acceptors, having no influence on the iodine-staining power of the digest.

The natural substrates for D-enzyme appear to be the maltodextrins, from maltotriose upwards. The power to act as donors (*i.e.*, as substrates for D-enzyme) of 16 sugars and sugar derivatives was tested and of these only one was attacked by D-enzyme. The full list is given in the Experimental section but they included glucose, methyl α-D-glucoside, maltose, *iso*maltose, and cellobiose. The exception was panose (6-*O*-α-D-glucosylmaltose). When this trisaccharide was treated with D-enzyme, it gave rise to two well-defined spots on a paper chromatogram, one moving in the pentasaccharide region, the other as a disaccharide. A trace of (?)glucose was also present.

The Rôle of Maltose.—It has already been mentioned that maltose, although it can act (inefficiently) as an acceptor, appears not to function as a donor in the transglycosylation catalysed by D-enzyme. Further, maltose is not produced, except in traces, when D-enzyme acts on the higher dextrins. It could be argued that D-enzyme does liberate maltose as a residue but that the latter is so efficient an acceptor that it does not accumulate in sufficient quantity to be detected. This is contradicted however by the observations (i) that maltose has only one-fifth of the efficiency of glucose in lowering the A.V. of D-treated maltopentaose, and (ii) that when an artificial mixture of maltose with higher dextrins was incubated with D-enzyme the maltose did not disappear.

It might further be argued that maltose is in fact a donor substrate for D-enzyme action but that the position of equilibrium is almost entirely on the maltose side. The only conceivable action of D-enzyme on maltose would be to convert it into maltotriose and glucose, the former being further disproportionated by D-enzyme. The addition of β-amylase to such a digest should, by degrading the maltotriose and higher dextrins, disturb the equilibrium in the direction of further disproportionation of the maltose. The net result of this sequence of reactions would be to convert the maltose into glucose. When, however, maltose was incubated with D-enzyme and β-amylase no such conversion into glucose occurred. It must be concluded that maltose cannot function as a donor in the D-enzyme system.

Discussion.—It appears from the foregoing that D-enzyme catalyses a transglycosylation, the substrate on which it acts (the donor) being a linear chain of glucose units joined

by α-1 : 4-linkages (exemplified by the maltodextrins). The enzyme shows marked specificity within the group of maltodextrins, a minimum chain-length of 3 being necessary in the substrate. Maltose appears not to be a donor. D-Enzyme, by the scission of an α-1 : 4-link, splits a maltodextrin chain into two fragments and transfers one of the fragments to an appropriate acceptor which, in the first stage of the reaction, is a molecule of the maltodextrin substrate. The enzyme is not so selective with respect to the acceptor molecule, glucose and maltose as well as the higher maltodextrins and other sugars being capable of functioning in this way. In every case however the junction effected between the transferred glycosyl radical and the acceptor molecule is by an α-1 : 4-glucosidic link. The net result when the enzyme acts on a maltodextrin is to produce a range of products of higher and lower molecular weight. The conclusion that the α-1 : 4-link is the only linkage synthesised in the transfer is based largely but not entirely on paper chromatographic evidence but it is completely confirmed by the work reported in the following paper. In essentials therefore the mode of operation of D-enzyme is the simultaneous breaking and making of α-1 : 4-linkages. The spread of molecular weight when equilibrium has been attained is directly related to the degree of polymerisation of the initial substrate. Thus maltotriose gives products which are stained orange by iodine (and then only when in high concentration) whereas maltotetraose and higher maltodextrins as substrates yield equilibrium mixtures of progressively greater intensities of staining. One explanation of this relation between degree of polymerisation of the initial substrate and the upper limit of chain length of the maltodextrins synthesised might lie in the assumption that equilibrium is reached when glucose is liberated (as a residue) as fast as it disappears (by accepting transferred glycosyl radicals). Since D-enzyme has no hydrolytic action the only source of glucose is the *reducing* end group of the maltodextrin substrate and the proportion of such end groups varies inversely with the degree of polymerisation of the substrate. It follows that an equilibrium concentration of glucose will be attained with less disproportionation of a short- than of a long-chain substrate and the average chain-length of the products will be smaller.

The anomalous position of maltose needs further investigation and this is proceeding. This sugar, although the first member of the maltodextrin series, cannot function as a donor, *i.e.*, its α-1 : 4-link is not attacked by the enzyme. Nevertheless a maltosyl radical can be transferred to an appropriate acceptor as is shown by the observation that the first products of the action of D-enzyme on maltotriose to be detected are glucose and maltopentaose. There is a suggestion here that the smallest glycosyl radical which can be transferred by D-enzyme contains two glucose units and that maltose fails to function as a donor because scission of the α-1 : 4-link would provide a radical for transfer consisting of a single glucose residue. If the usual assumption is made that the enzyme attacks from the non-reducing end of a maltodextrin chain, this statement is equivalent to saying that the terminal linkage at the non-reducing end is not susceptible to scission by D-enzyme.

It is more difficult to explain the non-appearance of maltose as a residual fragment in the transglycosylation process. One "explanation" would lie in the assumption that, for a reason at present unknown, the penultimate link at the *reducing* end of a maltodextrin chain is not susceptible to scission by D-enzyme; maltose could not then be liberated as a residue.

Comparison of D-Enzyme with Other Transglucosylases.—Two other enzymes are known which redistribute α-1 : 4-glucosidic linkages and D-enzyme is distinguishable from each. The amylase of *Bacillus macerans* has long been known to effect the synthesis of *cyclo*dextrins from starch. French, Levine, Norberg, Nordin, Pazur, and Wild (*J. Amer. Chem. Soc.*, 1954, **76**, 2387) have shown that the enzyme also catalyses the transfer of glycosyl radicals from these *cyclo*dextrins and from maltodextrins to acceptor molecules which include glucose, methyl α-D-glucoside, maltose, cellobiose, sucrose, and maltobionic acid. Maltose is, however, converted into maltotriose and glucose by this enzyme which is clearly less specific in its requirements than is D-enzyme.

Amylomaltase (Monod and Torriani, *Ann. Inst. Pasteur*, 1950, **78**, 65) is also distinguished from D-enzyme by the fact that it catalyses the synthesis of amylose-type polysaccharides from maltose, a reaction in which, as with D-enzyme, the amount of glucose

present controls the position of equilibrium. Xylose and mannose can also function as acceptors, as has been found to be the case with D-enzyme. It as evident that with both D-enzyme and amylomaltase a high degree of specificity with respect to the constitution and configuration of the " accepting " sugar unit is not observed.

Experimental

Concentrations of digest components are final values.

Methods.—Reducing powers were measured by the Somogyi copper reagent (*J. Biol Chem.*, 1945, **160**, 61) and when necessary the sugar solutions were deproteinised with Somogyi's reagents (*ibid.*, p. 69). Unless otherwise stated, iodine-staining was carried out by mixing 0·2 ml. of digest with 6 ml. of 0·005% iodine solution in 0·02% aqueous potassium iodide, the intensity of colour (A.V.) being measured in cells of 1·3 cm. diameter in an E. E. L. colorimeter with a No. 404 filter (wavelength of peak transmission = 510 mμ). Inorganic phosphate and phosphorylase activity determinations were made as in Part X (*J.*, 1950, 3566).

Paper-chromatographic fractionations of sugars were carried out on Whatman No. 54 paper with propan-1-ol–ethyl acetate–water (6 : 1 : 3, v/v) as irrigating solvent. When necessary, salts and protein were precipitated by mixing the sugar solution with 4 volumes of ethanol before applying the supernatant liquid to the paper. The positions of the sugars were located with benzidine–trichloroacetic acid (Bacon and Edelman, *Biochem. J.*, 1951, **48**, 114) or, when non-reducing carbohydrates were present, with silver nitrate–sodium hydroxide (Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444).

Materials.—*Maltodextrins.* These were prepared from potato amylose as by Whelan, Bailey, and Roberts (*J.*, 1953, 1293). The maltose used in the following experiments was material prepared in this way since commercial specimens contained a small amount of a trisaccharide. The concentrations of maltodextrins given refer to weights of products stored *in vacuo* over phosphoric oxide and usually containing at least 95% of carbohydrate.

Enzymes. α-Amylase was prepared from human saliva as by Whelan and Roberts (*J.*, 1953, 1298). The specimen used had a slight maltotriase activity. β-Amylase was the crystalline sweet-potato enzyme kindly provided by Dr. A. K. Balls. Potato phosphorylase was prepared as by Whelan and Bailey (*Biochem. J.*, 1954, **58**, 560), R-enzyme as in Part XIX (*J.*, 1954, 4440).

(*a*) Potato juice. Potatoes (300 g.) were peeled and sliced and either ground or minced with rapid incorporation of charcoal (10 g.) which had previously been boiled with water. It was important to produce an intimate mixture of potato pulp and charcoal as quickly as possible. The juice was expressed through muslin and centrifuged. The thick colloidal suspension of charcoal was removed from the supernatant solution by filtration through a silver-plated pressure filter and a series of two, or sometimes three, graded filters (KS, EK, and EK special, John Carlson Ltd., Ashton-under-Lyne, Lancs. The resulting juice was pale amber and did not darken over several days, but became red and eventually black when added to a dilute catechol solution.

(*b*) D-Enzyme. Ethanol (76·2 ml.) was added to potato juice (400 ml.) during 10 min. with stirring. The temperature, initially −2°, was allowed to fall to −5° as soon as sufficient alcohol was present to prevent freezing. This 16% ethanol precipitate was discarded on the centrifuge. Ethanol (43·4 ml.) was added at −5° and the 16—23% precipitate removed, dissolved in 0·01M-citrate buffer (pH 6·0; 400 ml.), and cooled to −2°, and the 16% and the 16—23% precipitate removed as above. The latter precipitate was dissolved in buffer (25 ml.), and the solution stored at 0°. The solution retained sufficient activity to be used up to 4 days from its preparation.

Proof that the Disproportionating Activity of the D-Enzyme Preparation is not due to Phosphorylase.—Phosphorylase solution (350 mg. of freeze-dried enzyme in 3·5 ml. of water) and D-enzyme solution were analysed for their inorganic phosphate contents; 1 ml. of each solution contained no detectable phosphate. The method is capable of detecting 5 μg. of phosphorus. The phosphorylase activities of each enzyme solution were determined, and two digests were prepared each containing 0·02M-maltopentaose and 0·038M-citrate buffer (pH 6·0). In addition one contained phosphorylase solution in 235-fold overall dilution; the other contained D-enzyme in 1·3-fold dilution. In this way both solutions contained equal phosphorylase activities. Portions (0·3 ml. each) of the digests were stained with iodine at intervals during incubation at 17°. The digests were each divided into two portions after 13 hr.; then one portion (1·2 ml.)

was mixed with potassium dihydrogen phosphate solution (0·2 ml., equiv. to 0·2 mg. of phosphorus) before continuing the incubation. The results are tabulated.

Comparison of D-enzyme and phosphorylase.

Time of incubation (hr.)	A.V. (510 mμ) D-Enzyme	D-Enzyme + phosphate	Phosphorylase	Phosphorylase + phosphate
3	4·8	—	0·0	—
4	6·6	—	0·0	—
7	12·1	—	0·0	—
8·5	15·2	—	0·0	—
13·25	—	18·3	0·0	0·0
19	29·0	20·8	0·3	0·0
31	36·5	25·5	3·3	2·1
60	43·5	31·3	9·4	6·5
80	45·5	34·0	14·2	10·0

Optimum Temperatures and pH *Values of D- and Q-Enzyme.*—(a) *D-Enzyme.* The digests of optimum pH contained D-enzyme solution in two-fold dilution, 0·017M-maltohexaose, and Michaelis's veronal buffer (*Biochem. Z.*, **1931**, **234**, 139) in three-fold dilution. Portions of each digest were stained with iodine after 2½ and 4½ hr. The values of A.V. (510 mμ) are plotted in Fig. 1. The digests at optimum temperature contained D-enzyme and substrate as above and 0·067M-citrate buffer (pH 6·7). After incubation at various temperatures for 45 and 90 min. portions were stained with iodine. The values of A.V. (510 mμ) are plotted in Fig. 2.

(b) *Q-Enzyme.* Digests of optimum pH contained 0·1% of amylose, D-enzyme in five-fold dilution, and veronal buffer in 1·66-fold dilution. Portions (0·1 ml.) of the digests were stained for measurement of A.V. (680 mμ) after 15 and 45 minutes' incubation at 15°. The digests at optimum temperature contained enzyme and amylose as above and 0·12M-citrate buffer (pH 6·7). Portions (0·1 ml.) of the digests were stained after incubation for 33 and 60 min. The results are given in Figs. 1 and 2.

Action of D-Enzyme on Glucose and Maltodextrins.—0·12M-Solutions of glucose and maltodextrins through to maltopentaose were prepared in D-enzyme solution containing 0·05M-citrate buffer (pH 7·0). Incubation was at 18° and at intervals portions of the digests were removed for fractionation on paper.

Successive Actions of D-Enzyme and α-Amylase on Maltotetraose.—The digest (50 ml.) contained D-enzyme in 3·33-fold dilution, maltotetraose ($4·45 \times 10^{-4}$ mole), and 0·048M-acetate buffer (pH 7·0) and was incubated at room temperature. Measurements of A.V. (510 mμ) of iodine stain after 0, 175, and 260 min. indicated that the intensity had increased from zero to a very nearly constant value of 10 colorimeter units. Measurements of reducing power were also made at these times on deproteinised portions of the digest. The reducing equivalents of 0·2 ml. portions of digest were, respectively, 2·31, 2·34, and 2·37 ml. of 0·005N-thiosulphate. At 260 min. the whole digest was heated at 100° for 3 min., then cooled and filtered, and a portion (27·5 ml.) was treated with α-amylase solution (3·6 ml.; 150 mg.) at 35° under toluene. After 12 hours' incubation the enzyme was inactivated by heat, a portion (1 ml.) removed for paper chromatography, and the remainder, equivalent to $2·37 \times 10^{-4}$ mole of original maltotetraose, fractionated on charcoal–Celite as decribed by Whelan *et al.* (*loc. cit.*). Only three sugars were eluted. These were chromatographically identical with glucose, maltose, and maltotriose. Paper-chromatographic fractionation of the whole digest similarly revealed only these sugars. The amounts of the sugars eluted were calculated by summation of the optical rotations of the fractions, using the $[\alpha]_D$ values reported by Whelan *et al.* (*loc. cit.*). These amounts were $1·56 \times 10^{-4}$, $2·38 \times 10^{-4}$, and $1·00 \times 10^{-4}$ mole, respectively, equivalent to $2·30 \times 10^{-4}$ mole of maltotetraose, *i.e.*, 97% of the material fractionated on the column.

Simultaneous Actions of β-Amylase and D-Enzyme on Maltotriose.—Two digests (3 ml. each) contained 0·033M-maltotriose, 0·083M-citrate buffer (pH 7·0), and crystalline β-amylase (*ca.* 20 units). In addition, one digest contained D-enzyme in 2·5-fold dilution. After incubation for 4 and 17 hr. at room temperature portions of the digests were removed for fractionation on paper. The results are described in the Discussion section.

Effect of Addition of Glucose to the D-Enzyme–Maltohexaose System when in Equilibrium.—The digest (3 ml.) contained 0·017M-maltohexaose, 0·083M-citrate buffer (pH 6·0), and D-enzyme in two-fold dilution. Iodine-staining was carried out as usual during 10 hours' incubation at 20°;

a portion of the digest (0·9 ml.) was then added to glucose (30 mg.), and iodine staining carried out on both portions of the digest. The results are shown in Fig. 3.

Possible Alternative Substrates for D-Enzyme.—Potato juice (2 ml.) was added to 50 mg. of each of the following sugars and the digests were incubated for 18 hr. at 18°; whereafter portions were inactivated by heat and fractionated on paper: D-glucose, D-fructose, L-sorbose, D-rhamnose, D-ribose, D-sorbitol, DL-erythritol, D-mannitol, sucrose, *iso*maltose, lactose, melibiose, αα-trehalose, cellobiose, methyl α-D-glucoside, and panose. For results see p. 48.

Incorporation of [^{14}C]Glucose into Maltodextrins.—Radioactive starch from tobacco leaves (20 mg.) was hydrolysed for 2 hr. with sulphuric acid as described by Pirt and Whelan (*J. Sci. Food Agric.*, **1951**, **2**, 224), neutralised with barium hydroxide, and evaporated to 0·05 ml. A digest containing 0·03M-maltopentaose, 0·05M-citrate buffer, and D-enzyme in two-fold dilution was incubated at pH 7·0 and 20° until the maximum intensity of iodine staining was attained; then a portion (1·2 ml.) equivalent to $0{\cdot}36 \times 10^{-4}$ mole of substrate was mixed with 0·4 ml. of the hydrolysed starch solution. After incubation for 55 hr. under toluene at 20° a portion (0·2 ml.) of the digest was treated with alcohol to remove salts and protein, and half the material transferred to a paper chromatogram for fractionation. An equivalent quantity of hydrolysed starch was fractionated on the same paper, and also an artificial mixture of maltodextrins and the hydrolysed starch. After development and location of the sugars the radioactivity associated with each of the sugar spots was determined by Dr. L. H. May. The total counts/min. in the two controls were 979 and 1059 respectively; 731 counts/min. were recovered from the digest. The results showed that no exchange of activity occurred between glucose and maltodextrins in the artificial mixture but that in the digest activity had disappeared from the glucose zone and was approximately accounted for by the appearance of activity in the zones associated with the maltodextrins.

Sugars as Acceptors in the D-Enzyme–Maltopentaose System in Equilibrium.—A digest (6·2 ml.) containing 0·097M-maltopentaose, 0·03M-citrate buffer (pH 7·0), and D-enzyme in 1·2-fold dilution was incubated at room temperature until a constant intensity of iodine staining was reached; then portions (0·5 ml.) were transferred to solutions (0·2 ml.) each containing 25 mg. of one of the following sugars: glucose, maltose, methyl α-D-glucoside, xylose, mannose, fructose, sucrose, and αα-trehalose. A further portion (0·5 ml.) was mixed with 0·2 ml. of water. Iodine staining was carried out after further incubation for 0·45, 6·45, and 19 hours. The results are described on p. 48.

Synthesis of a Non-dialysable Polysaccharide.—A digest (50 ml.) containing 0·01M-maltohexaose, 0·02M-citrate buffer (pH 7·0), and D-enzyme in 4·1-fold dilution was incubated at 18° until iodine staining indicated that equilibrium was attained (14 hr.). Measurements of reducing power of deproteinised samples after 0·1, 3, and 14 hr. gave the following values (ml. of 0·005N-thiosulphate per ml. of digest): 10·96, 10·43, and 10·04 respectively. The remainder of the digest was heated at 100° for 3 min., then dialysed against distilled water (4 × 1 l.) during 3 days, with continual stirring of the external solution. The impermeable material was filtered through a Seitz pad, to remove protein, and freeze-dried, yielding 78 mg. of a white product which did not migrate on a paper chromatogram.

Properties of the Synthetic Polysaccharide.—A solution of the polysaccharide of known concentration (method of Pirt and Whelan, *loc. cit.*) was treated with the Somogyi copper reagent (*loc. cit.*) at 100° for 1 and 1·5 hr. (cf. Whelan *et al.*, *loc. cit.*). Titration of the cuprous oxide after these times gave 0·005N-thiosulphate equivalents of 1·27 ml. and 1·34 ml. respectively per 1·94 mg. of polysaccharide [as $(C_6H_{10}O_5)_n$]. From the average of these two values it was calculated that the average degree of polymerisation of the polysaccharide was 12·1. β-Amylolysis at pH 4·8 followed by paper-chromatographic fractionation revealed only maltose and maltotriose. D-Enzyme in 3·5-fold dilution was incubated in 0·08M-citrate buffer (pH 7·0) with 0·005M-polysaccharide at 20° and iodine staining carried out at intervals. The following changes in intensity (colorimeter units) and colour were noted [the time of measurement (hr.) precedes the A.V. (510 mμ)]: 0, 63·2 (red); 0·25, 71·5 (red); 1, 83·0 (deep red); 2·25, 113·6 (purple); 5, 125·6 (violet); 21, 114·5 (purple).

Action of D-Enzyme on Amylopectin.—Two digests were prepared, containing 0·5% of waxy maize starch, 0·04M-citrate buffer (pH 7·0), and D-enzyme in 3·3-fold dilution; one digest contained 0·27M-glucose. Iodine staining was carried out at intervals during incubation at 20°. The results are given in Fig. 3. After 20 hr. portions of the digests were examined on a paper chromatogram. No sugars were detected in the enzyme + amylopectin digest, but the digest containing glucose contained maltotriose.

Simultaneous Actions of β-Amylase and D-Enzyme on Maltose.—These experiments were

carried out in the same way as when maltotriose was used as substrate; two digests were prepared, one containing only D-enzyme, the other containing D-enzyme and β-amylose. Paper chromatography of the digests showed that D-enzyme, neither by itself nor in combination with β-amylase, had any effect on the maltose other than to produce a trace of glucose after prolonged incubation (25 hr.).

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11. *The Enzymic Synthesis and Degradation of Starch. Part XXI.* The Dextrins synthesised by D-Enzyme.*

By STANLEY PEAT, W. J. WHELAN, and (the late) G. W. F. KROLL.

The dextrins synthesised by the action of D-enzyme on maltotriose have been isolated and shown to be products containing only α-1 : 4-glucosidic linkages. A convenient and economic method of preparing pure maltodextrins is thus provided.

IT was shown in Part XX * that potato D-enzyme reversibly disproportionates maltotriose and the higher maltodextrins. The question there left open whether *only* α-1 : 4-linkages are synthesised by D-enzyme, has been re-examined by the isolation of the pure glucose polymers, thus produced from maltotriose.

Maltotriose, prepared from potato starch by α-amylolysis with human salivary amylase, was treated with D-enzyme and the products were separated on charcoal–Celite as described by Whelan, Bailey, and Roberts (*J.*, 1953, 1293). Maltodextrins containing 1—6 glucose units were thus isolated, with higher polymers which were not further examined. The yields are shown in the Table and the low relative yield of maltose should be noted. Paper

Properties of products of D-enzyme action on maltotriose.

Fraction	Yield * (g.)	$[\alpha]_D$ in H_2O †	β-Acetate †: M. p.	β-Acetate †: $[\alpha]_D$ in $CHCl_3$	Hydrolysis by β-amylase (%) ‡
Monosaccharide ...	1·52	+52·0° (+52·6°)	131° (131°)	+3·1° (+3·8°)	—
Disaccharide	0·143	+137·6° (+136°)	157° (159°)	+62·8° (+63°)	—
Trisaccharide	1·95	+158·9° (+160°)	133° (135°)	+85·2° (+86°)	0
Tetrasaccharide ...	1·48	—	—	—	97·2 (97·5)
Pentasaccharide ...	1·23	—	—	—	102·9 (101·6)
Hexasaccharide ...	0·676	—	—	—	99·7 (99·4)

* From 10 g. of maltotriose.

† Values for authentic specimens are given in parentheses.

‡ Values for the tetra- and the hexa-saccharide are calculated in terms of theoretical maltose, for the pentasaccharide in terms of its conversion into an equimolar mixture of maltose and maltotriose. The values for authentic specimens of the maltodextrins refer to products obtained from amylose as by Whelan *et al.* (*loc. cit.*) and were measured by Dr. P. J. P. Roberts.

chromatography indicated that the mono-, di-, and tri-saccharide fractions contained only glucose, maltose, and maltotriose respectively. Sufficient is now known of the chromatographic behaviour of *iso*maltose, *iso*maltotriose, and the trisaccharides containing both α-1 : 4- and α-1 : 6-linkages, *e.g.*, panose, to be sure that none of these substances was present in detectable amount. In addition, each fraction from the di- to the hexa-saccharide obeyed the linear R_M–molecular weight relation which exists between members of the maltodextrin series (Whelan *et al.*, *loc. cit.*). The mono-, di-, and tri-saccharides were rigidly identified by the $[\alpha]_D$ values of the free sugars and the properties of their crystalline β-acetates. Further, the tetra-, penta-, and hexa-saccharides were pure maltodextrins since each was completely hydrolysed by β-amylase, which is specific for

* Part XX, preceding paper.

α-1 : 4-glucoside scission. The properties of the D-enzyme products and their derivatives are shown in the Table.

These results prove that the digestion of maltotriose with D-enzyme yields a mixture consisting of glucose, unchanged maltotriose, and the higher maltodextrins. Maltose is also produced, but relatively very little, and it is questionable whether it is a true product of D-enzyme action since its occurrence, as revealed by paper chromatographic fractionation of D-treated maltodextrins, is not always observed. The production of maltose by the particular enzyme preparation used here was apparent when the whole maltotriose digest was examined by paper chromatography but the question whether the pure enzyme is capable of producing maltose remains unsettled.

These experiments provide a very convenient means of preparing pure maltodextrins in quantity, better than our earlier preparation by partial acidic hydrolysis of amylose (Whelan *et al.*, *loc. cit.*). The substrate, maltotriose, is more easily prepared than is amylose, which must be carefully purified to avoid the possibility of contamination by amylopectin, for an impure amylose would give maltodextrins contaminated with branched dextrins. Again, only about one-sixth of the maltotriose substrate is converted by D-enzyme into glucose and maltose, whereas the optimum conditions for the liberation of maltotriose and the higher dextrins from amylose result in losses of up to half of the substrate as the unwanted mono- and di-saccharides. Moreover, the possibility of contamination of the maltodextrins from amylose with acid-reversion products (from glucose) is non-existent in the enzymic method. The method is also economical. Untreated saliva is used to prepare maltotriose from starch and the fact that some of the maltotriose is hydrolysed by an enzymic impurity in the saliva is of little consequence since the starch substrate is inexpensive. The D-enzyme preparation required for the experiment is simply the twice-precipitated protein fraction of potato juice soluble in 16%, but insoluble in 30%, ethanol.

Experimental

Preparation of Maltotriose.—Potato starch (125 g., wet) was made into a paste with cold water (500 ml.) and added during 15 min. to boiling 0·1% aqueous sodium chloride (3·3 l.). Vigorous stirring and boiling were maintained for an additional 45 min. and the solution was then cooled rapidly in cold water. 0·2M-Sodium acetate buffer (50 ml.; pH 4·8) was added, followed by the supernatant solution from a mixture of human saliva (25 ml.) and water (25 ml.) which had been allowed to stand for 1 hr. before centrifugation. The digest was diluted to 4 l., covered with toluene, and incubated at 30°. Pirt and Whelan's method (*J. Sci. Food Agric.*, 1951, **2**, 224) showed that 97·2 g. of starch were present. After incubation for 3 days the digest was boiled for a few minutes to destroy the enzyme. (Subsequent experiments have shown that incubation for 1 day is sufficient.) The supernatant liquid was adsorbed on a charcoal–Celite column (100 × 8·5 cm.). The column was irrigated with water, and then 7·5% and 15% ethanol as described by Whelan *et al.* (*loc. cit.*). The optically active material eluted by 15% ethanol contained traces of maltose and glucose; it was therefore refractionated by the same procedure (column size, 80 × 4·5 cm.) and 10·5 g. of chromatographically pure maltotriose were obtained.

Preparation of D-Enzyme.—Charcoal-treated potato juice (preceding paper) (400 ml.) was placed in a bath at −5° and when the juice had cooled to −2° ethanol (76·2 ml.) was added with mechanical stirring during 10 min. After 10 min. at −5° the precipitate was removed on a centrifuge at −5° and to the supernatant solution at −5° were added a further 94·8 ml. of ethanol. The precipitate formed, after being kept for 10 min. at −5°, was recovered by centrifugation and dissolved in 0·01M-citrate buffer (100 ml.; pH 7·0).

Action of D-Enzyme on Maltotriose.—The enzyme solution (45 ml.), 0·2M-citrate buffer (20 ml.; pH 7·0), and maltotriose (10 g.) were mixed and diluted to 100 ml. with water. The digest was incubated at room temperature for 16·5 hr. After inactivation of the enzyme by heat, the cooled digest was passed through a Seitz filter to remove coagulated protein and then transferred to a charcoal–Celite column (80 × 4·5 cm.) which was eluted as described by Whelan *et al.* (*loc. cit.*) except that the ethanol was added by the gradient method (cf. Alm, Williams, and Tiselius, *Acta Chem. Scand.*, 1952, **6**, 826), 33% ethanol being added through a constant-level device to a mechanically stirred reservoir of water (4 l.) which led to the column. By comparison with the stepwise addition of ethanol, this method provides an improved fractionation of the maltodextrin products, separation of mono- to tetra-saccharides being absolute.

The products as far as the hexasaccharide were recovered as described by Whelan *et al.* (*loc. cit.*); the higher dextrins were eluted by passing 50% ethanol through the column. A control experiment in which the enzyme preparation was adsorbed on a charcoal column and eluted with water and aqueous ethanol showed that no sugars were derived from this source.

Characterisation of the Products.—Measurements of $[\alpha]_D$ of the mono-, di-, and tri-saccharides were made by the method employed by Whelan *et al.* (*loc. cit.*); the β-acetates of these sugars were prepared by sodium acetate–acetic anhydride. β-Amylolysis of the tri-, tetra-, penta-, and hexa-saccharides was carried out as follows. Solutions of the dextrins of known concentration were prepared as by Whelan *et al.* (*loc. cit.*). These were incorporated in digests containing dextrin (*ca.* 16 mg.), purified soya-bean β-amylase (1·5 ml.; 35 units; Part XVI, *J.*, 1952, 714), and 0·2M-sodium acetate buffer (1·5 ml.; pH 4·8) in a total volume of 11 ml. Incubation was at 30° and portions (1 ml. each) of the digests were removed after 1·5, 2·5, and 3·5 hr. for determination of reducing power. Digests containing (i) maltose in place of dextrins and (ii) only enzyme and buffer served as controls on the maltase activity and reducing power of the enzyme. The results, corrected for the slight maltase activity, showed that the hydrolysis of the tetra-, penta, and hexa-saccharides was complete after 1·5 hr. and no further change took place. The trisaccharide fraction was not attacked. The digest contents were also examined by paper chromatography in butan-1-ol–acetic acid–water (4 : 1 : 5 by vol.), it being expected that the digests of the tetra- and the hexa-saccharide would show only maltose and that of the pentasaccharide only maltose and maltotriose (cf. Whelan and J. G. Roberts, *Biochem. J.*, 1954, **58**, 569). These inferences were confirmed except that the tetra- and hexa-saccharide digests contained minute traces of tetrasaccharide, and the latter also a very small amount of trisaccharide, agreeing with the appearance of a trace of pentasaccharide in the original hexasaccharide fraction.

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12. *Infrared Spectra and the Polymorphism of Glycerides. Part I.*

By D. CHAPMAN.

The infrared spectra of the different polymorphic forms of some 1- and 2-monoglycerides have been obtained between 3500 and 650 cm.$^{-1}$. Information about the polymorphic transitions and about the molecular structure of the polymorphic forms has been obtained, *e.g.*, the stability of the α-form and the crystallinity of the sub-α-form of the 1-monoglycerides.

ALTHOUGH it is known that abrupt changes can occur in the infrared spectra of the crystalline phase when polymorphic transitions occur (Kendall, *Analyt. Chem.*, 1953, **25**, 382; Tyler and Ehrhardt, *ibid.*, p. 390; Keller and Halford, *J. Chem. Phys.*, 1949, **17**, 26), little use has been made of this to investigate polymorphic transitions themselves, in molecules such as fatty acids, esters, and glycerides. The present paper reports an investigation of the polymorphism of some monoglycerides carried out by means of infrared spectra.

Whilst infrared spectra of some monoglycerides have been reported (Kuhrt, Welsh, Blum, Perry, and Weber, *J. Amer. Oil Chemists' Soc.*, 1952, **29**, 261; Barcelo and Martin, *J. Phys. Radium*, 1954, **5**, 403; O'Connor, Dupre, and Feuge, *J. Amer. Oil Chemists' Soc.*, 1955, **32**, 88), none of this work was concerned with the various polymorphic forms, and the spectra given there are mainly solution spectra or those of the stable β-form. Up to the present, spectra of 2-monoglycerides have not been reported.

Experimental.—Samples of 1-monostearin (m. p. 81°), 1-monopalmitin (m. p. 77°), and 1-monolaurin (m. p. 63°) were obtained by the action of the corresponding acyl chloride (from pure fatty acids) on redistilled *iso*propylideneglycerol and recrystallised slowly from acetone or ether–acetone by Mr. M. Dallas of this laboratory. The samples of 2-monolaurin (m. p. 51·0°), 2-monomyristin (m. p. 61·3°), 2-monopalmitin (m. p. 68·5°), and 2-monostearin (m. p. 75·5°) were presented by Dr. A. G. Tallentire of Bristol University.

The infrared spectrometer was a Grubb-Parsons S.3 double-beam spectrometer with a rock-salt prism. The spectra were obtained between 3500 and 650 cm.$^{-1}$. A heated infrared cell was used for the investigation of the liquid and for the polymorphic transitions which occur on heating or cooling. A thermocouple was arranged and calibrated so that the temperature of the material could be determined to $\pm 1°$. Capillary thicknesses of the glycerides between rock-salt flats were investigated. The β′- and the β-forms of 1-monoglycerides were obtained by rapid and slow crystallisation from light petroleum respectively. The spectra of these forms were obtained by dispersion in Nujol. The identities of the sub-α, β′-, and β-forms were confirmed by m. p. and *X*-ray data. The β-forms of the 2-monoglycerides were obtained by crystallisation from the melt and also by solvent crystallisation.

Results and Discussion.—1-*Monoglycerides.* The pioneer work of Malkin and Shurbagy (*J.*, 1936, 1628) showed that 1-monoglycerides exist in three different solid modifications, *viz.*, a low-melting α-form and two higher-melting forms, β′ and β. The α-form is thought to be one in which the chains are vertical and rotating. The *X*-ray powder photograph of this form shows only one strong side spacing at 4·12 Å and it is uniaxial. Hydrocarbons (Müller, *Proc. Roy. Soc.*, 1932, *A*, **138**, 514), alcohols (Bernal, *Z. Krist.*, 1932, **83**, 153), and esters (Malkin, *Trans. Faraday Soc.*, 1933, **29**, 977) possess analogous α-forms

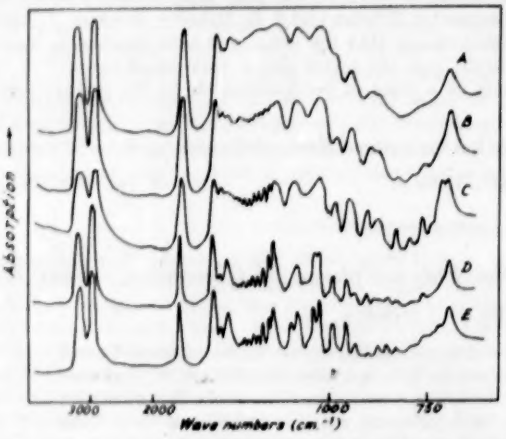


FIG. 1. *Polymorphic forms of* 1-*monostearin.*
A, Liquid; *B*, α; *C*, sub-α; *D*, β′; *E*, β.

with vertical rotating chains. They all have a side spacing of 4·12 Å and are uniaxial. Lutton and Jackson (*J. Amer. Chem. Soc.*, 1948, **70**, 2445) have claimed the existence of a fourth form, sub-alpha. They suggest that the α-form is reasonably stable down to a lower transition temperature at which point it changes reversibly into a new crystalline modification, sub-α, giving a distinctive set of short spacings. Controversy exists, however, whether the sub-α-form is or is not crystalline, whether the sub-α to α-transformation is genuinely reversible and whether in fact the α-form is stable down to the lower transition temperature (Malkin, "Progress in the Chemistry of Fats and Other Lipids," Pergamon Press, London, 1954, Vol. II).

1-*Monostearin liquid form.* The infrared spectra of 1-monostearin in the liquid state and in the various polymorphic forms are shown in Fig. 1.

In the spectrum of the liquid the bands are typically broad and have a tendency to smear into each other. The OH absorption band at 3453 cm.$^{-1}$ indicates that hydrogen bonding of the hydroxyl groups is occurring. The C=O stretching absorption band occurs at 1706 cm.$^{-1}$.

Assignment of other bands in the spectrum is more difficult. Both C–O stretching and O–H deformation vibrations of the alcohol groups in the glycerides might be expected to give rise to strong absorption bands since most alcohols do in fact give rise to two bands. However, confusion exists even in the spectra of alcohols as to their correct assignment (Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 94).

A broad strong band at 1174 cm.$^{-1}$ may however be assigned to a C–O stretching vibration of the CO_2R group since a band at this frequency occurs in all glycerides, whilst bands at 1048 and 975 cm.$^{-1}$ are probably associated with primary alcohol groups. A band near 935 cm.$^{-1}$ is probably associated with secondary alcohol groups (cf. O'Connor *et al.*, *loc.cit.*). A band at 719 cm.$^{-1}$ can be certainly associated with a methylene rocking mode.

1-*Monostearin α-form.* When the liquid is cooled to the α-melting point, crystallisation was visually observed and a change occurred in the spectrum (see Fig. 1). This form is the α-form. A series of bands now occurs in the 1180—1340 cm.$^{-1}$ region, which can be assigned to CH_2 wagging modes by analogy with similar bands which have been observed in the solid state of *n*-paraffins (Brown, Sheppard, and Simpson, *Discuss. Faraday Soc.*, 1950, **9**, 261), long chain fatty acids (Jones, McKay, and Sinclair, *J. Amer. Chem. Soc.*, 1952, **74**, 2575), αω-polymethylenedicarboxylic esters (Gunthardt, 1st. Reunion Molecular Spectroscopy, Paris, 1953), and alkyl bromides (Brown and Sheppard, *Trans. Faraday Soc.*, 1954, **50**, 535) and shown by the latter to arise from CH_2 wagging modes. The OH absorption band shifts to 3360 cm.$^{-1}$ but remains broad and the carbonyl absorption band shifts to 1721 cm.$^{-1}$. From this it can be deduced that the OH group becomes more strongly hydrogen-bonded in the α-form than was the case in the liquid state, but that the reverse occurs with the carbonyl group. This suggests that in the liquid state hydrogen bonding occurs between OH and C=O groups but that in the solid form bonding is preferentially between OH groups.

The strong bands near 1111 and 1048 cm.$^{-1}$ remain relatively unchanged, but slightly increased resolution of other bands occurs and a number of new weak bands appear.

The band at 719 cm.$^{-1}$ assigned to a CH_2 rocking mode becomes more intense and sharper than the same band in the liquid spectrum. Since the general broadness of bands observed in the spectrum is more typical of a liquid than a normal crystalline solid, the spectrum of the α-form is consistent with the existence of rotating hydrocarbon chains in this form.

On further cooling, little change occurs in the α-form spectrum apart from a slight increase in resolution of the bands, until 47° is reached. The α-form is therefore reasonably stable from the α-form melting point down to the sub-α-form melting point and this is in agreement with the *X*-ray observation by Lutton and Jackson (*loc. cit.*).

1-*Monostearin sub-α-form.* At this point the sub-α-form is obtained and a change occurs in the spectrum. The major change is the splitting of the single band at 719 cm.$^{-1}$ of the α-form spectrum, into two (at 727 and 719 cm.$^{-1}$). An analogous situation occurs with solid *n*-paraffins in this region of the spectrum and throws some light on the situation. In the liquid state of the paraffins a single band is observed near 720 cm.$^{-1}$; this band increases in intensity but remains single at the solidification point. At a lower transition point two components occur (Robert and Favre, *Compt. rend.*, 1952, **234**, 2270). Between the solidification and transition points the paraffins exist in a hexagonal form and rotation of the hydrocarbon chains about their axes takes place. This can be compared with the α-form of the monoglycerides. Below the transition point the crystal system becomes orthorhombic (Müller, *loc. cit.*). In Polythene an analogous band (725 cm.$^{-1}$) is single in the amorphous or liquid state, but double in the crystalline form. A more detailed examination of the doublet has been given recently by Stein and Sutherland (*J. Chem. Phys.*, 1954, **22**, 1993) who showed that the splitting arises in *n*-paraffins and Polythene in the solid form only when these materials are in a certain crystalline state. Stein (*ibid.*, 1955, **23**, 734) describes the doublet in terms of interaction between nearest-neighbour CH_2 groups, the CH_2 rocking frequency in the isolated molecule ν_0 being split into two components, the out-of-phase component being at a frequency very slightly higher than ν_0, and the in-phase component at a considerably higher frequency. This definitely suggests that the sub-α-form has a crystalline lattice (or at least a very ordered system), and this is in agreement with Lutton and Jackson's conclusion (*loc. cit.*). It might also be predicted that the unit cell in the sub-α-form is smaller than that in the α-form (cf. Stein, *loc. cit.*).

Other changes between the spectra of the α- and the sub-α-form are that the OH band shifts from *ca.* 3360 cm.$^{-1}$ in the α-form to *ca.* 3342 cm.$^{-1}$ in the sub-α-form, and the carbonyl

band shifts from 1721 to 1730 cm.$^{-1}$. The OH group therefore again becomes more strongly hydrogen-bonded whilst the reverse occurs with the carbonyl group. The bands between 852 and 727 cm.$^{-1}$ also become better resolved. The spectrum in general suggests some orientational freedom since the general sharpness of bands typical of the spectrum of normal crystalline material does not occur, and this orientational freedom appears a little greater nearer the melting point of the sub-α-form than at room temperature. This is consistent with the work of Crowe and Smyth (*J. Amer. Chem. Soc.*, 1950, **72**, 4427), who observed orientational freedom in the sub-α-form and suggested that orientation of various molecular segments occurred in order to explain the wide distribution of relaxation times observed in the sub-α-phase despite the order observed by *X*-ray methods.

The sub-α-form was observed to be quite stable at room temperature, in agreement with the observation of Lutton and Jackson (*loc. cit.*). Further, by heating the sub-α-form to 47° the α-form was again observed. This transformation from one form to the other was observed to occur repeatedly. The reversible effect with the α- and sub-α-forms and indeed the stability of the α-form itself may, however, depend on the presence or absence of sufficient β′- or β-nuclei.

Although a transition temperature at 42° is reported (Malkin, *op. cit.*), little change occurred in the spectrum of the sub-α-form below 47° except for a slight increase in resolution of some bands.

1-*Monostearin* β′- *and* β-*forms*. The β′- and the β-spectrum obtained from a dispersion in Nujol are very similar to each other and are more typical of the type of spectrum normally obtained with true crystalline materials, *i.e.*, bands are narrow and sharp. The β′-form was obtained by rapid crystallisation. The rapid-crystallisation technique sometimes gives a mixture of forms although the β′-form is generally predominant. The *X*-ray powder photograph can indicate whether any β-form is present since the short spacings of the β′- and the β-form are quite different, but it is difficult to ascertain whether any sub-α-form is present because of the similarity of the short spacings.

In the β′-form spectrum the OH absorption band is split into components at 3342 (the main component) and 3243 cm.$^{-1}$. The carbonyl band occurs at 1736 cm.$^{-1}$, and the broad band at 1050 cm.$^{-1}$ observed in the sub-α-form spectrum is split into two components (at 1062 and 1047 cm.$^{-1}$). The 1181 cm.$^{-1}$ band is now quite sharp and a band at 1100 cm.$^{-1}$ is almost resolved into different components. A number of small bands occur in the region between 850 and 729 cm.$^{-1}$, which may be due to rocking modes of the methylene groups by analogy with hydrocarbon spectra (Brown and Sheppard, *loc. cit.*). There is only one component at 719 cm.$^{-1}$.

In the β-form spectrum the OH stretching band is again split into two components. The main component is at 3243 cm.$^{-1}$ with the other at 3307 cm.$^{-1}$. Near 1100 cm.$^{-1}$ there are clearly three components and the bands at 1063 and 1048 cm.$^{-1}$ are slightly more split than in the β′-form spectrum. There is again only one component of the methylene rocking absorption band, at 719 cm.$^{-1}$. The spectra of the β-form have been discussed in more detail by Barcelo and Martin (*loc. cit.*). It is of interest that whilst with *X*-ray powder photographs it is easy to distinguish between β- and β′-forms but difficult to distinguish between the β′- and the sub-α-forms, with infrared spectra it is easy to distinguish between sub-α- and β′-forms but difficult to distinguish between β′- and β-forms.

It is perhaps significant that the OH stretching band moves to lower frequencies (showing that an increase in the strength of the hydrogen bonding is occurring) in the order liquid ⟶ α ⟶ sub-α ⟶ β′ ⟶ β. This is also the order of stabilities of the polymorphic forms. The existence and stability of these polymorphic forms may therefore be bound up with the hydrogen-bonding schemes possible, and the strength of the hydrogen bonding to the hydroxyl groups.

1-*Monopalmitin*. Similar results were obtained with 1-monopalmitin. The α-form gives rise to a spectrum similar to that observed with 1-monostearin. The α-form was quite stable down to the sub-α-transition temperature, at which point the sub-α-form was observed, giving rise to a spectrum similar to that of the sub-α-form of 1-monostearin. This sub-α-form was stable at room temperature, but did change during several weeks at this temperature into the β′-form. When the sub-α-form was heated above the transition

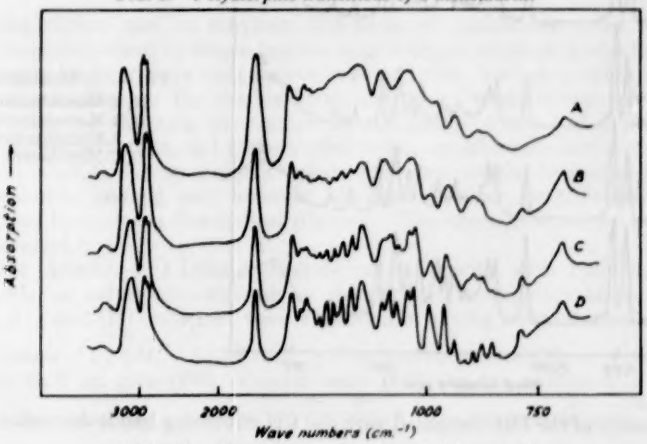
temperature the α-form could be obtained. The β′- and the β-form were obtained by crystallisation from solvents.

1-*Monolaurin*. With 1-monolaurin the sub-α-form was not observed since the transition temperature for this glyceride was below room temperature. At room temperature, transition to the stable β-form was observed to occur within a few hours (Fig. 2).

The spectra of monoglycerides of different chain length in the same polymorphic form were quite similar, except for the number of methylene wagging bands which increase as the chain length increases. This is similar to the situation with spectra of crystalline fatty acids (Jones *et al.*, *loc cit.*).

2-*Monoglycerides*. The only thermal investigation of 2-monoglycerides is due to Daubert and Clarke (*Oil and Soap*, **1945**, **22**, 113) who concluded that they were not polymorphic. Malkin (*op. cit.*), however, suggests that 2-monoglycerides probably separate from the melt in the α-form but change extremely rapidly into the β-form. *X*-Ray data, however, of only one form have been obtained (Filer, Sidhu, Daubert, and Longenecker, *J. Amer. Chem. Soc.*, **1946**, **68**, 167).

FIG. 2. *Polymorphic transitions of* 1-*monolaurin*.



A, Liquid; *B*, α; *C*, α ⟶ β′; *D*, β′ ⟶ β.

2-*Monomyristin liquid*. The OH stretching absorption band in the liquid form of 2-monomyristin is at 3527 cm.$^{-1}$ and so the OH group is not very strongly bound in the liquid state. The carbonyl absorption band is at 1715 cm.$^{-1}$.

A band at 1175 cm.$^{-1}$ may be assigned to a C–O stretching vibration of the CO_2R group. Bands occur at 1048 and 975 cm.$^{-1}$ (cf. 1-monoglycerides) which are perhaps associated with the primary alcohol groups. A band at 720 cm.$^{-1}$ can be assigned to a methylene rocking vibration.

2-*Monomyristin* β-*form*. As the liquid 2-monoglyceride cooled, the first form to crystallise was the stable β-form and no evidence for an α-form was observed. (The spectrum of the material crystallised from solvent and shown by *X*-rays to be the β-form was observed to be identical with this.)

The OH frequency in the β-form shifts to 3347 cm.$^{-1}$, showing that the OH group has become more strongly hydrogen-bonded than in the liquid state, whilst the C=O absorption band is at 1733 cm.$^{-1}$, showing the carbonyl group has become less strongly bonded (cf. 1-monoglycerides). In view of the difference in frequency of the OH stretching absorption bands in the β-form of 1- and 2-monoglycerides it is of interest that the 2-monoglycerides, which on grounds of symmetry might have been expected to melt higher than the 1-isomers, melt several degrees lower. The frequency is higher for the 2- than for the 1-monoglycerides, and therefore the hydrogen bonding to the OH groups is stronger in the

latter. A regular series of bands between 1344 and 1184 cm.$^{-1}$ (cf. 1-monoglycerides) can be assigned to methylene wagging modes.

A band at 975 cm.$^{-1}$ is greater in relative intensity compared with the 1048 cm.$^{-1}$ band in the spectrum of the β-form of 2-monoglyceride than is the case with the corresponding 1-mono-glyceride (there are two primary alcohol groups in the 2-monoglycerides, and one primary alcohol group in the 1-monoglycerides). The region from 780 to about 700 cm.$^{-1}$ is unusual in that a broad absorption extends over the whole of this range with bands at 736 and 720 cm.$^{-1}$ (assigned to methylene rocking modes), apparently superposed on the general absorption. This does not occur in the spectra of other glycerides or esters.

The spectra of 2-monoglycerides of different chain length are very similar (Fig. 3), the main difference being the number of the bands in the 1350—1184 cm.$^{-1}$ range. The

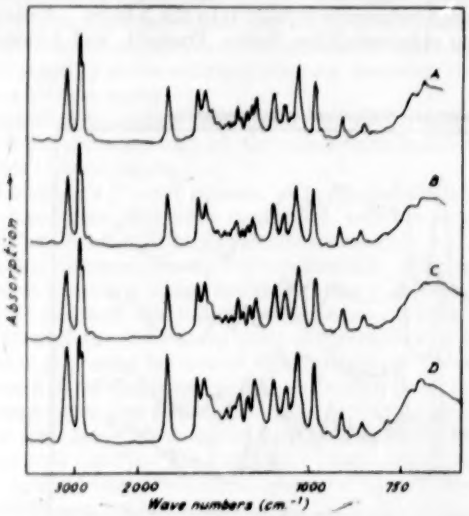


FIG. 3. *2-Monoglycerides.*
A, 2-Monostearin.
B, 2-Monopalmitin.
C, 2-Monomyristin.
D, 2-Monolaurin.

relative intensity of the OH compared with the CH stretching bands decreases as the chain length increases.

Whilst heating the 2-monoglycerides it was observed that a transition to the corresponding 1-monoglyceride took place. Acyl migration in 2-monoglycerides is known to take place in the presence of a catalyst (Stimmel and King, *J. Amer. Chem. Soc.*, **1934**, **56**, 1724) but not by the action of heat alone. If, however, *e.g.*, 2-monolaurin is held a few degrees above its melting point for three hours, the infrared spectrum shows that almost complete conversion into the 1-monolaurin takes place. A similar change was observed to occur with the other 2-monoglycerides examined.

In conclusion, the investigation has shown that infrared spectra can provide a good standard for observing and following polymorphic transitions. This method for studying polymorphic transitions has some advantages over the *X*-ray method, notably the speed of obtaining the spectra and the information from them about the bonding of the groups. As a supplement to the *X*-ray technique it is of obviously great potential value.

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13. *Addition of Free Radicals to Unsaturated Systems. Part XII.* Free-radical and Electrophilic Attack on Fluoro-olefins.*

By R. N. Haszeldine and J. E. Osborne.

The ease of electrophilic reaction of iodine monochloride, hydrogen iodide, or hydrogen bromide with certain fluoro-olefins decreases in the order $CF_2{:}CH_2$ > $CF_2{:}CFCl$ > perfluoro*cyclo*butene > perfluoro*cyclo*hexene > $CF_3{\cdot}CF{:}CF{\cdot}CF_3$. The ease of free-radical reaction of hydrogen bromide, bromine, chlorine, or trifluoroiodomethane decreases in the order $CF_2{:}CH_2$ > $CF_2{:}CF_2$ > $CF_2{:}CHCl$ > $CF_2{:}CFCl$ > $CF_3{\cdot}CF{:}CF_2$ > $CF_3{\cdot}CF{:}CF{\cdot}CF_3$ > perfluoro*cyclo*butene > perfluoro*cyclo*hexene.

Syntheses of a variety of chloro-, bromo-, iodo-, and trifluoromethyl-*cyclo*butanes, -*cyclo*butenes, -*cyclo*hexanes, and -*cyclo*hexenes are described. The mode of reduction of polyfluoro-compounds by lithium aluminium hydride, and the rearrangement of fluoro-carbanions are considered.

Unsubstituted olefins such as ethylene, but-2-ene, or *cyclo*hexene react readily with electrophilic reagents such as hydrogen halides, to give simple addition products. Replacement of hydrogen by fluorine in such molecules should slow down or prevent electrophilic addition by deactivation of the double bond and/or by steric effects. A qualitative comparative study of the ease of reaction of the fluoro-olefins 1 : 1-difluoroethylene, 2-chloro-1 : 1-difluoroethylene, and perfluoro-but-2-ene, -*cyclo*hexene, and -*cyclo*butene has been made (*a*) with the electrophilic reagents hydrogen iodide, hydrogen bromide, or iodine monochloride, and (*b*) with bromine, hydrogen bromide, or trifluoroiodomethane under conditions favouring a free-radical reaction. The effect of structure on reactivity can thus be assessed.

Electrophilic Attack.—1 : 1-Difluoroethylene reacts readily with hydrogen bromide, hydrogen iodide, or iodine monochloride in the dark at room temperature to give the products (I), (II), and (III) expected from a reaction involving ionic intermediates and an olefin polarisation $\overset{\delta+}{C}F_2{=}\overset{\delta-}{C}H_2$. 2-Chloro-1 : 1-difluoroethylene combines with hydrogen iodide in the dark to give (IV), isomeric with (III), to the exclusion of its isomer $CHF_2{\cdot}CHClI$, thus revealing a polarisation $\overset{\delta+}{C}F_2{=}\overset{\delta-}{C}HCl$; the reaction is much slower than

$CF_2Br{\cdot}CH_3$	$CF_2I{\cdot}CH_3$	$CF_2Cl{\cdot}CH_2I$	$CF_2I{\cdot}CH_2Cl$
(I)	(II)	(III)	(IV)

that with 1 : 1-difluoroethylene. The structures of these compounds follow from their boiling points, chemical evidence (see Experimental section), and ultraviolet spectra shown in the Table.

Ultraviolet spectra in light petroleum.

	$\lambda_{max.}$	ε	$\lambda_{min.}$	ε		$\lambda_{max.}$	ε	$\lambda_{min.}$	ε
$CF_2Cl{\cdot}CF_2I$	272	295	215	17	*$CH_3{\cdot}CF_2I$	267	340	207	10
$CF_3{\cdot}CF_2{\cdot}CF_2I$	271	240	215	13	*$CF_2Cl{\cdot}CH_2I$	263	500	212	20
$CF_2{\cdot}CF_2I$	270	—	—	—	$CF_2{\cdot}CH_2I$	262	265	—	—
$CF_2{\cdot}CH_2{\cdot}CF_2I$	271	290	219	24	$CF_2{\cdot}CH_2{\cdot}CH_2I$ ...	261	375	213	20
*$CH_2Cl{\cdot}CF_2I$	269	340	228	55	$CH_3{\cdot}CH_2I$	258	435	215	20
*$CHFCl{\cdot}CF_2I$	269	290	223	40					

* Prepared during present work. Other spectra taken from *J.*, 1953, 1764.

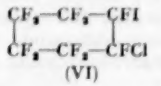
The maximum in the ultraviolet spectrum of a compound $R{\cdot}CF_2I$ varies from 267 mμ when R = alkyl to 271 mμ when R = perfluoroalkyl, whereas a compound $R{\cdot}CH_2I$ has a maximum between 258 mμ (R = alkyl) and 262 mμ (R = perfluoroalkyl). Ultraviolet spectra can thus be used to distinguish between $R{\cdot}CF_2I$ and $R{\cdot}CH_2I$ and it is clear that the compounds marked with an asterisk in the Table have the structures shown rather than

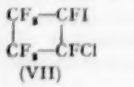
* Part XI, Haszeldine and Steele, *J.*, 1955, 3005.

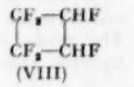
those which would result from ionic addition in the opposite sense. The cases where R in $R{\cdot}CF_2I$ is $\cdot CH_2Cl$ or $\cdot CHFCl$ fit well into the series, and it is evident that substitution of hydrogen on the β-carbon atom of $\overset{\alpha}{C}\text{–}\overset{\beta}{C}I$ by fluorine causes a shift to longer wavelength, and that the shift is more marked when hydrogen or fluorine on the β-carbon is replaced by halogen other than fluorine. A similar effect is observed in the series $R{\cdot}CH_2I$.

The olefins perfluorobut-2-ene, perfluoro*cyclo*hexene, and perfluoro*cyclo*butene are markedly resistant to electrophilic attack. Thus they fail to react with hydrogen bromide or iodide even at temperatures above 200°. Reaction of iodine monochloride with perfluorobut-2-ene gives only the dichloride (V); under similar conditions perfluoro*cyclo*hexene yields mainly its dichloride and only small amounts of the iodine chloride adduct (VI). By contrast, perfluoro*cyclo*butene gives mainly the adduct (VII), and for reactions involving ionic intermediates the ease of addition is thus *cyclo*-C_4F_6 > *cyclo*-C_6F_{10} > C_4F_8.

$CF_3{\cdot}CFCl{\cdot}CFCl{\cdot}CF_3$ (V)


(VI)


(VII)


(VIII)

Since it has recently been shown(*J.*, 1955, 3880) that perfluoro*cyclo*butene rearranges during reaction with hydrogen iodide, the structure of (VI) and (VII) was proved, to ensure that similar rearrangement had not occurred. Photochemical chlorination of the product (VI) gave 1 : 2-dichlorodecafluoro*cyclo*hexane which is of known constitution. Photochemical chlorination of the *cyclo*butane analogue (VII) similarly gave the known 1 : 2-dichlorohexafluoro*cyclo*butane, and reaction of (VII) with lithium aluminium hydride gave 1 : 1 : 2 : 2 : 3 : 4-hexafluoro*cyclo*butane (VIII); the absence of rearrangement during the reduction was shown by conversion of (VIII) into 1 : 2-dichlorohexafluoro*cyclo*butane, and thence into perfluoro*cyclo*butene.

Free-radical Addition.—Exposure of a mixture of 1 : 1-difluoroethylene and hydrogen bromide to ultraviolet light of wavelength >2200 Å produces 2-bromo-1 : 1-difluoroethane (IX) by a free-radical chain reaction :

$$Br\cdot + CH_2{:}CF_2 \longrightarrow CH_2Br{\cdot}CF_2\cdot \xrightarrow{HBr} CH_2Br{\cdot}CHF_2 + Br\cdot \longrightarrow \text{etc.}$$

Free-radical attack is exclusively on the CH_2 group and this agrees with the direction found for attack by a trifluoromethyl radical (*J.*, 1954, 923). The photochemical reaction of hydrogen bromide in light of wavelength >3000 Å gives approximately equal amounts of (I) and (IX), *i.e.*, the ionic and the free-radical reaction proceed at about the same rate under these conditions.

The order *cyclo*-C_4F_6 > *cyclo*-C_6F_{10} > C_4F_8 observed for electrophilic attack above is changed for free-radical attack, since perfluorobut-2-ene reacts most readily with hydrogen bromide on exposure to light, to give a mixture of the hydrogen bromide adduct (X) and the

$CH_2Br{\cdot}CHF_2$ (IX) $\qquad$ $CF_3{\cdot}CHF{\cdot}CFBr{\cdot}CF_3$ (X) $\qquad$ $(CF_3)_2CF{\cdot}CFI{\cdot}CF_3$ (XI)

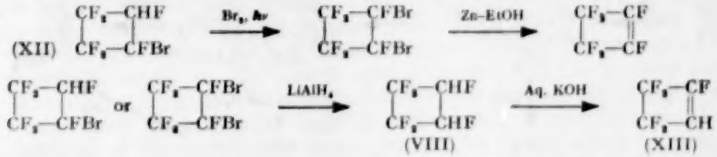
dibromide. Reaction is very slow relatively to that of fluoroethylenes, and considerably slower than for unsubstituted ethylenes or butenes, and the formation of the dibromide is caused by photolysis of hydrogen bromide to give free bromine which then undergoes a slow photochemical reaction with the double bond. There is no indication of the isomerisation :

$$CF_3{\cdot}CF{:}CF{\cdot}CF_3 \xrightarrow{Br} CF_3{\cdot}CFBr{\cdot}\dot{C}F{\cdot}CF_3 \rightleftharpoons CF_3{\cdot}CF_2{\cdot}\dot{C}F{\cdot}CF_2Br \xleftarrow{Br} CF_3{\cdot}CF_2{\cdot}CF{:}CF_2$$

during photochemical reaction of bromine with perfluorobut-1- or -2-ene (cf. the rearrangement of fluoro-carbanions discussed below). Perfluorobut-1-ene reacts much faster with bromine than does perfluorobut-2-ene, as observed by Brice, LaZerte, Hals, and Pearlson (*J. Amer. Chem. Soc.*, 1953, **75**, 2698). Photochemical chlorination of perfluorobut-2-ene is much more rapid than bromination.

Trifluoroiodomethane reacts smoothly but slowly with perfluorobut-2-ene to give 2-iodo-3-trifluoromethyloctafluorobutane (XI). The attack of the trifluoromethyl radical on the olefin is markedly slower than it is on perfluoropropene (*J.*, 1953, 3559).

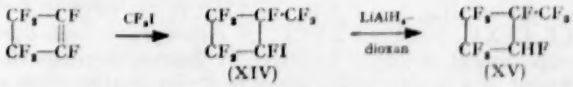
Perfluoro*cyclo*butene reacts with hydrogen bromide even less readily than perfluorobut-2-ene to give 1-bromo-1 : 2 : 2 : 3 : 3 : 4-hexafluoro*cyclo*butane (XII) (first described by Park, Sharrah, and Lacher, *J. Amer. Chem. Soc.*, 1949, **71**, 2339) and somewhat larger amounts of the dibromide. That rearrangement had not occurred during photochemical reaction (cf. reaction with hydrogen iodide, Haszeldine and Osborne, *J.*, 1955, 3880) is shown by the following reactions :



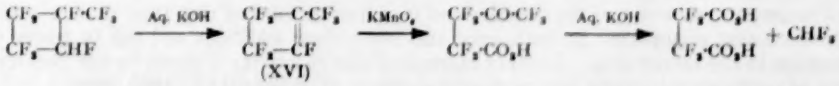
Replacement of bromine by hydrogen was effected smoothly by use of lithium aluminium hydride, which was recently employed (Tatlow and Worthington, *J.*, 1952, 1251; Buxton and Tatlow, *J.*, 1954, 1177) for replacement of chlorine by hydrogen in mono- and di-chloropolyfluoro*cyclo*hexanes, and for the reduction of 1 : 2-dichlorohexafluoro*cyclo*butane to (VIII).

Both bromine and chlorine react with perfluoro*cyclo*butene on exposure to ultraviolet light, and that free-radical rearrangement has not occurred during formation of the 1 : 2-dibromo- or 1 : 2-dichloro-compounds is shown by debromination or dechlorination to perfluoro*cyclo*butene, and by reduction to 1 : 1 : 2 : 2 : 3 : 4-hexafluoro*cyclo*butane (VIII). The removal of the last traces of ethyl ether from the product (VIII) (b. p. 27°) was accomplished by treatment with boron trifluoride which combines with ether but not with the fluorocarbon. The structure of the product (VIII) was established by oxidation with alkaline permanganate, since perfluorosuccinic acid was produced, probably by way of 1 : 3 : 3 : 4 : 4-pentafluoro*cyclo*butene (XIII) (cf. Buxton and Tatlow, *loc. cit.*). Two CF_2 groups must thus be adjacent.

Trifluoroiodomethane reacts slowly but smoothly with perfluoro*cyclo*butene to give 1-iodo-2-trifluoromethylhexafluoro*cyclo*butane (XIV). The iodine was readily replaced by chlorine, and both the iodo- and the chloro-compound were reduced by lithium aluminium hydride in dioxan :



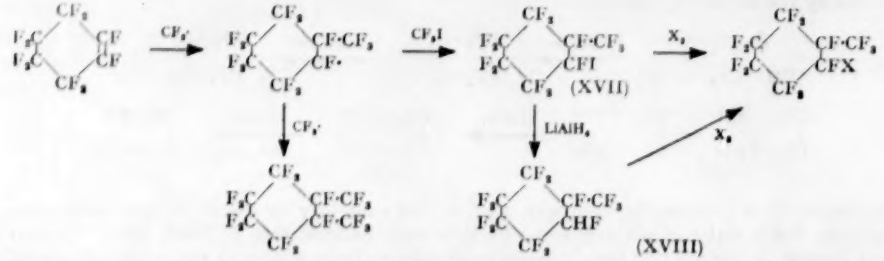
Reaction of 1-trifluoromethyl-1 : 2 : 2 : 3 : 3 : 4-hexafluoro*cyclo*butane (XV) with aqueous potassium hydroxide gave 2-trifluoromethyl*cyclo*butene (XVI) which yields a dichloride. Alkaline permanganate oxidised the *cyclo*butene (XVI) to perfluorosuccinic acid *via* the keto-acid, which was not isolated; perfluorosuccinic acid and fluoroform, produced by alkaline cleavage of the keto-acid, were also obtained from (XV) :



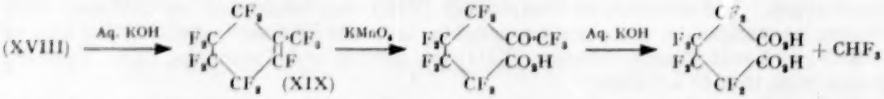
These reactions adequately prove the structures of the compounds (XIV), (XV), and (XVI).

Perfluoro*cyclo*hexene does not react at all with hydrogen bromide on irradiation at room temperature under the conditions used for perfluorobut-2-ene and perfluoro*cyclo*butene. Photochemical bromination or chlorination can be effected by prolonged irradiation, and that rearrangement had not occurred was shown by conversion of the 1 : 2-dibromo- and 1 : 2-dichloro-decafluoro*cyclo*hexanes into perfluoro*cyclo*hexene in good yield.

Trifluoroiodomethane reacts very slowly with perfluoro*cyclo*hexene, but prolonged irradiation gave a satisfactory yield of 1-iodo-2-trifluoromethyldecafluoro*cyclo*hexane (XVII), from which the 1-bromo- and 1-chloro-compound were made by photochemical halogenation. As by-product with (XVII) was obtained perfluoro-1 : 2-dimethyl*cyclo*-hexane. This is clearly produced by combination of the intermediate radical with a CF_3 radical, the first time that this addition of two CF_3 radicals to a double bond has been observed. The fluorocarbon had previously been prepared by direct fluorination of *o*-xylene.



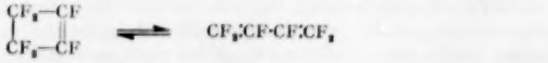
Reduction of the iodo-compound (XVII) gives (XVIII), which can be chlorinated to give 1-chlorodecafluoro-2-trifluoromethyl*cyclo*hexane, and reaction of the last compound with aqueous potassium hydroxide yields nonafluoro-1-trifluoromethyl*cyclo*hexene (XIX); this forms a dibromide and a dichloride. Only one olefin is formed, and this demonstrates that a tertiary fluorine atom is removed by aqueous base in preference to a secondary one; this was also shown by the formation of only one olefin from the analogue (XV). Alkaline permanganate oxidises the compounds (XVIII) and (XIX) to perfluoroadipic acid *via* the keto-acid, which was not isolated :



The isolation of perfluoroadipic acid shows that four CF_2 groups are adjacent, and proves the structure of the compounds (XVII), (XVIII), and (XIX).

By comparison with olefins studied earlier (*J.*, 1953, 1199, 1592, 3559, *et seq.*) the following qualitative order for ease of ***radical*** attack can be given C_2H_4, $CH_3{\cdot}CH{:}CH_2$, $CH_3{\cdot}CH{:}CH{\cdot}CH_3$, *cyclo*-$C_6H_{10}$ > $CF_2{:}CH_2$ > $CF_2{:}CF_2$ > $CF_2{:}CHCl$ > $CF_2{:}CFCl$ > $CF_3{\cdot}CH{:}CF_2$ > $CF_3{\cdot}CF{:}CF_2$ > $CF_3{\cdot}CF{:}CF{\cdot}CF_3$ > *cyclo*-C_4F_6 > *cyclo*-C_6F_{10}. It is thus evident that (*a*) replacement of vinylic hydrogen by fluorine decreases the ease of radical attack, (*b*) attachment of a perfluoroalkyl group to a vinyl-carbon atom causes a marked decrease in ease of radical attack, and (*c*) a double bond in a four- or six-membered ring is less readily attacked by a free radical than that in a straight-chain olefin. All of these effects can be attributed to electron withdrawal by fluorine, particularly by perfluoroalkyl groups adjacent to the double bond ($CF_3 \leftarrow CF{:}CF \rightarrow CF_3 \longleftrightarrow F^-CF_2{:}\overset{+}{C}F{\cdot}CF_3$, etc.), and to steric inhibition of attack.

The greater reactivity of the double bond in a four-membered ring than that in a six-membered ring is apparent in both ionic and free-radical additions and can be traced to the strain in the former ring. Another example of this reactivity is given by the isomerisation of perfluoro*cyclo*butene into perfluorobutadiene when heated (*J.*, 1955, 3880) :



Perfluoro*cyclo*hexene does not show an analogous reaction.

Nucleophilic Attack during Reductions by Lithium Aluminium Hydride.—The marked ease of replacement of chlorine, bromine, or iodine by hydrogen in polyfluoro*cyclo*-butanes

or -hexanes by use of lithium aluminium hydride merits comment, since such replacement by use of conventional reducing agents is extremely difficult if not impossible. It is suggested that the effectiveness of lithium aluminium hydride in this connection is due to (*a*) use of ether as a solvent and (*b*) the fact that hydride-ion attack on carbon can occur despite the powerful shielding effect of the fluorine atoms. Of these, (*b*) is by far the more important.

Ether probably plays a part by forming a weak molecular complex $RX{\cdot}OEt_2$ with the chlorine or bromine in RX of the (Lewis) acid–(Lewis) base type. Such complex formation has been demonstrated with polyfluoroiodo-compounds (*J.*, 1953, 2622) and with polyfluorobromo-compounds (unpublished results), and doubtless plays an important rôle in the formation of perfluoroalkyl Grignard compounds (*J.*, 1952, 3423; 1953, 1748; 1954, 1273) from perfluoroalkyl iodides by making the iodine more readily removable as an iodide ion.

If nucleophilic attack on the carbon atom of a molecule (*A*) is considered, where X = Cl, Br, or I, and R = perfluoroalkyl, the fluorine atoms ought to facilitate such attack, since by their inductive effect they should increase the positive character of the carbon atom and so enhance the ease of attack by a negative ion. Normally this effect, which would enable rapid nucleophilic replacement of X to occur, is more than offset by two factors: (i) the decrease in the ease with which X^- can be lost as the final stage of a bimolecular reaction:

(*A*)

$$Y^- + R{\cdot}CF_2{-}X \longrightarrow [Y\cdots\cdots CF_2\cdots\cdots X] \longrightarrow Y{-}CF_2R + X^-$$

this is again a direct consequence of the inductive and hyperconjugative effects of the fluorine atoms; (ii) the shielding of the carbon by the small but remarkably effective strongly electronegative fluorine atoms which both by their steric effect and by their field effect adequately prevent access of the nucleophilic reagent to the carbon atom. It is thus suggested that lithium aluminium hydride acts as source of hydride ion which, by virtue of its small size, can overcome the factor (ii) above:

$$H^- + R{\cdot}CF_2{-}X \longrightarrow R{\cdot}CHF_2 + X^-$$

The attack doubtless occurs through hydride-ion shift in a cyclic complex, possibly of the type postulated for hydride-ion shift during the reduction of carbonyl compounds by Grignard solutions (*J.*, 1953, 1748), and it is not suggested that free hydride ions are present in ethereal lithium aluminium hydride. The ready replacement of halogen by hydrogen in *cyclo*-butanes or -hexanes by use of lithium aluminium hydride supports the above ideas, since shielding of the carbon by the attached fluorine atoms is decreased in the cyclic compounds and ease of attack by H^- is thereby increased. If the above ideas are correct it is clear that the stability of perfluorocarbons is due more to the shielding effect than to the negativity of the fluorine atoms.

Fluoro-carbanion Rearrangement.—The conversion of a fluoro-acid into an olefin containing a terminal double bond by pyrolysis of its anhydrous sodium salt:

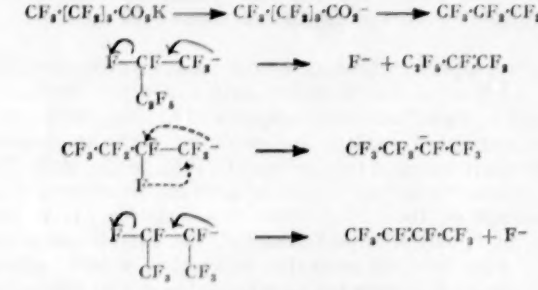
$$CF_3{\cdot}[CF_2]_n{\cdot}CF_2{\cdot}CF_2{\cdot}CO_2Na \longrightarrow CF_3{\cdot}[CF_2]_n{\cdot}CF{:}CF_2 + NaF + CO_2$$

has been established as a general reaction capable of application to acids containing chlorine as well as fluorine, and to dibasic acids (*Nature*, 1951, **168**, 1028; *J.*, 1952, 4259; 1954, 4026; 1955, 3880; see Brice *et al.*, *loc. cit.*, for reference to American work). Brice *et al.* studied the effect of variation of the metal on the course of the pyrolysis, and noted that potassium perfluoropentanoate gave two olefins:

$$CF_3{\cdot}[CF_2]_2{\cdot}CO_2K \longrightarrow CF_3{\cdot}CF{:}CF{\cdot}CF_3\ (80\%) + CF_3{\cdot}CF_2{\cdot}CF{:}CF_2\ (20\%)$$

Our independent work, done in order to study the preparation of the perfluorobut-2-ene required for the reactions described above, is in agreement with this result, except that the ratio of the olefins obtained (approx. 1 : 1) is appreciably different. The important

fact is that two olefins are obtained, however, and this we interpret as evidence for fluorocarbanion rearrangement (see *Nature*, **1951**, **168**, 1028, for the original suggestions about fluorocarbanion reactivity) :



This suggests that potassium fluoride must act as catalyst for the fluoro-carbanion isomerisation, whereas sodium fluoride does not, and some support for this is given by the fact that pyrolysis of an equimolar mixture of sodium and potassium perfluoropentanoate gives essentially the same ratio of perfluorobut-2-ene to perfluorobut-1-ene (**47** : **45**) as does pyrolysis of the potassium salt alone (**48** : **43**), whereas pyrolysis of the pure sodium salt yields only perfluorobut-1-ene. If the potassium salt decomposed preferentially, the potassium fluoride so produced might react with sodium perfluoropentanoate by a solid-state reaction to give more potassium salt :

$$KF + C_4F_9{\cdot}CO_2Na \rightleftharpoons C_4F_9{\cdot}CO_2K + NaF$$

Pyrolysis of the potassium salt would thus displace this equilibrium to the right.

Potassium fluoride does not catalyse the rearrangement of perfluorobut-1-ene into the but-2-ene, so rearrangement must occur before the olefin is formed. Studies of the salt of acids of longer chain length will be reported later.

Experimental

Reactions were carried out in sealed Pyrex or silica tubes unless otherwise stated. Precautions were taken to exclude air, moisture, or material which might catalyse ionic or free-radical reactions. The olefins used were spectroscopically pure and free from peroxides, and were distilled *in vacuo* before use. Reaction products were manipulated in a conventional vacuum system.

Reactions of **1** : **1**-*Difluoroethylene.*—(a) ***With hydrogen iodide.*** The olefin (**1·7** g.) and anhydrous hydrogen iodide (**6·0** g.), kept at **20°** in the dark (**6** days), gave **1** : **1**-*difluoro*-**1**-*iodoethane* (**5·0** g., **98%**), b. p. **45°**, n_D^{19} **1·4183** (Found : C, **12·2**; H, **1·8%**; *M*, **193**. $C_2H_3IF_2$ requires C, **12·5**; H, **1·6%**; *M*, **192**). The isomeric **1** : **1**-difluoro-**2**-iodoethane boils at **89·5°** (Booth and Burchfield, *J. Amer. Chem. Soc.*, **1935**, **57**, **2070**). The above reaction time was unnecessarily long, and subsequent experiments showed that reaction is rapid (**2** hr.) even at **−30°**, particularly if solid iodine, which catalyses the reaction, is added.

(b) ***With hydrogen bromide.*** Difluoroethylene (**1·71** g.) and hydrogen bromide (**2·28** g.), kept at **20°** in the dark (**95** hr.), gave **1**-*bromo*-**1** : **1**-*difluoroethane* (**3·9** g., **100%**), b. p. **14·4°** (isoteniscope) (Found : C, **16·3**; H, **2·3%**; *M*, **144**. $C_2H_3BrF_2$ requires C, **16·6**; H, **2·1%**; *M*, **145**). The isomeric **2**-bromo-**1** : **1**-difluoroethane, which boils at **57·3°** (Henne and Midgley, *ibid.*, **1936**, **58**, **884**), was not formed.

The difference in b. p. of **44°** between the isomers $CF_2X{\cdot}CH_3$ and $CHF_2{\cdot}CH_2X$ (X = I or Br) is noteworthy; a similar effect is apparent when X = Cl (cf. $CF_2Cl{\cdot}CH_3$, b. p. **−9°**, and $CHF_2{\cdot}CH_2Cl$, b. p. **35°**).

(c) *Photochemical reaction with hydrogen bromide.* The olefin (**0·68** g.) and hydrogen bromide (**0·95** g.), irradiated in a silica tube (**1·2** hr.), gave unchanged starting materials (**10%**), **2**-bromo-**1** : **1**-difluoroethane (**1·3** g., **85%** based on olefin), b. p. **56·5—57·0°** (Found : *M*, **145**), and only a very small amount of **1**-bromo-**1** : **1**-difluoroethane produced by an ionic reaction.

In a second experiment, difluoroethylene (1·54 g.) and hydrogen bromide (1·90 g.) in a Pyrex tube (which cuts off light of wavelength <3000 Å) were irradiated for 17 hr., to give unchanged starting materials (30%), 2-bromo-1 : 1-difluoroethane (1·12 g.), b. p. 57·0—57·5° (Found : *M*, 145), and 1-bromo-1 : 1-difluoroethane (1·13 g.), b. p. 14—15° (Found : *M*, 145).

(d) *With iodine monochloride.* Difluoroethylene (1·11 g.) and iodine monochloride (2·10 g.), kept in the dark (4 days) at room temperature, gave unchanged olefin (0·26 g.) and *1-chloro-1 : 1-difluoro-2-iodoethane* (2·90 g., 74% based on olefin), b. p. 97·5°, n_D^{20} 1·465 (Found : C, 10·5; H, 1·0. $C_2H_2ClIF_2$ requires C, 10·6; H, 0·9%). The direction of addition is shown by the ultraviolet spectra and by the fact that the infrared spectrum of the product differs from that of its isomer described below. The product was uncontaminated by its isomer.

Reaction of 2-Chloro-1 : 1-difluoroethylene with Hydrogen Iodide.—The olefin (0·73 g.) and hydrogen iodide (0·90 g.), kept at 30° (1 day), gave only 0·05 g. of product, b. p. >0°. In a second experiment, the olefin (3·11 g.) and hydrogen iodide (2·3 g.) were kept at 20° (6 days), to give 0·72 g. of product of b. p. >0°. The combined products were distilled, giving only *2-chloro-1 : 1-difluoro-1-iodoethane*, b. p. 101°, n_D^{18} 1·468 (Found : C, 10·5; H, 1·1. $C_2H_2ClIF_2$ requires C, 10·6; H, 0·9%).

The direction of addition follows from the reaction of the chlorofluoroiodoethane (0·43 g.) with zinc (0·7 g.) and ethanol (0·7 ml.) in a sealed tube at 20° (19 hr.) to give only 1 : 1-difluoroethylene (80%) (Found : *M*, 64. Calc. for $C_2H_2F_2$: *M*, 64), identified by means of its infrared spectrum. The ultraviolet spectrum of the iodo-compound is also in accord with the proposed structure.

Reaction of Perfluorocyclohexene.—(a) *With hydrogen halides.* The olefin (2·4 g.) and hydrogen bromide (0·8 g.), heated at 240—250° (22 hr.), failed to react and the hydrogen bromide was recovered unchanged.

Hydrogen iodide (1·19 g.), perfluoro*cyclo*hexene (2·45 g.), and iodine (0·2 g.; to act as catalyst), heated at 240—250° (22 hr.) and then distilled *in vacuo*, gave unchanged hydrogen iodide (87%) and perfluoro*cyclo*hexene, examination of which by ultraviolet spectroscopy failed to detect any iodo-compound possibly present in low concentration.

Irradiation of perfluoro*cyclo*hexene (2·5 g.) and hydrogen bromide (1·6 g.) in a silica tube at room temperature (12 days) gave unchanged hydrogen bromide (63%), hydrogen, bromine, and the perfluoro*cyclo*hexene. Careful examination of the last material failed to reveal the presence of bromo-compounds. This does not necessarily mean that hydrogen bromide will not react photochemically with perfluoro*cyclo*hexene, but only that it fails to react under conditions where the other olefins studied will react.

(b) *With chlorine or bromine.* The olefin (2·8 g.) and a slight excess of chlorine, shaken in a silica tube and exposed to ultraviolet light (25 hr.), gave 1 : 2-dichlorodecafluoro*cyclo*hexane (81%), b. p. 109°, m. p. 37°, and unchanged olefin (15%). The dichloro-compound was spectroscopically identical with a known specimen. Roylance, Tatlow, and Worthington (*J.*, 1954, 4426) report m. p. 39—41° for this compound. Perfluoro*cyclo*hexene and chlorine react only slowly in the dark at the temperature used for the photochemical chlorination (50°).

The olefin and bromine similarly react only very slowly at room temperature or at 80° in the absence of light. Exposure of perfluoro*cyclo*hexene (2·9 g.) and bromine (20% excess) in a silica tube to intense ultraviolet light (48 hr.) at 80° gave unchanged olefin (1·0 g.) and 1 : 2-dibromodecafluoro*cyclo*hexane (83% based on olefin used), micro-b. p. 139°, m. p. 30—32° after sublimation. Tatlow and Worthington (*J.*, 1952, 1251) report b. p. 140°, m. p. 32°.

The 1 : 2-dichloro- and -dibromo-decafluoro*cyclo*hexane prepared as above were combined and heated (90°) and shaken with zinc (4 g.) and ethanol (15 ml.) in a sealed tube (8 hr.), to give perfluoro*cyclo*hexene (85%), spectroscopically identical with a known specimen.

(c) *With iodine monochloride.* Mixtures of perfluoro*cyclo*hexane (3·0—5·5 g.) and iodine monochloride (2·2—4·7 g.) were heated in sealed tubes under a wide variety of conditions of temperature (50—205°), reactant ratio, and time. In most cases where reaction occurred at all, approx. 65% of the perfluoro*cyclo*hexene was recovered, and 30% of it was converted into the dichloride, b. p. 110°. Small quantities of an iodo-compound with a b. p. higher than 110° were detected in reactions at the higher temperatures (150—200°). The fractions of highest b. p. from all the experiments were combined and distilled, to give *1-chloro-2-iododecafluoro-cyclohexane* (0·2 g., 1%), micro-b. p. 140° (Found : C, 16·7. C_6ClIF_{10} requires C, 16·9%).

A similar series of experiments gave the 1-chloro-2-iododecafluoro*cyclo*hexane, (micro-) b. p. 142°, in 3% yield. The compound (0·9 g.) was mixed with a 10% excess of chlorine in a sealed 5 ml. tube, which was kept in the dark (4 days), then exposed to ultraviolet light

(24 hr.). Distillation gave **1** : 2-dichlorodecafluoro*cyclo*hexane (78%), spectroscopically identical with a known specimen.

(d) *With trifluoroiodomethane.* Perfluoro*cyclo*hexene (4·2 g.) and trifluoroiodomethane (100% excess) were exposed to intense ultraviolet radiation from a Hanovia lamp 2 cm. from the silica reaction tube. Even with this vigorous treatment and a temperature of 60—65°, the reaction was very slow, and after 24 days 70% of the olefin was recovered unchanged. The material with b. p. >60° was removed and the unchanged trifluoroiodomethane and perfluoro-*cyclo*hexene were again irradiated (3 weeks). Distillation of the combined products gave unchanged olefin (44%), *decafluoro*-1-*iodo*-2-*trifluoromethyl*cyclo*hexane* (68% based on olefin used), (micro-) b. p. 132° (Found: C, 18·3%; *M*, 455. C_7IF_{13} requires C, 18·3%; *M*, 458), and perfluoro-1 : 2-dimethyl*cyclo*hexane (11% based on olefin used), b. p. 101—102° (Found: C, 24·0%; *M*, 400. Calc. for C_8F_{14}: C, 24·0%; *M*, 400). Haszeldine and Smith (*J.*, 1950, 2689) report b. p. 100—102° for the perfluorodimethyl*cyclo*hexane.

*Some Reactions of Polyhalogeno-trifluoromethyl*cyclo-*hexanes and -hexenes.*—The reactions of chloropolyfluoro*cyclo*hexanes with lithium aluminium hydride have been studied by Tatlow and Worthington (*J.*, 1952, 1251).

(*a*) To a stirred solution of lithium aluminium hydride (1·0 g.) in dry ether (20 ml.) was slowly added (2 hr.) decafluoro-1-iodo-2-trifluoromethyl*cyclo*hexane (4·1 g.) in dry ether (10 ml.). After being kept (1 hr.) and heated under reflux (1 hr.) the excess of lithium aluminium hydride was destroyed by cautious addition of 25% sulphuric acid (10 ml.), followed by water (30 ml.). The dried ethereal layer and extracts of the aqueous solution were distilled to give 1-H-*decafluoro*-2-*trifluoromethyl*cyclo*hexane* (62%), b. p. 86° (isoteniscope) (Found: C, 25·2; H, 0·3%; *M*, 330. C_7HF_{13} requires C, 25·3; H, 0·3%; *M*, 332).

(*b*) A mixture of 1-*H*-decafluoro-2-trifluoromethyl*cyclo*hexane (3·1 g.), potassium hydroxide (1·5 g.), and water (3 ml.) was heated in a sealed tube at 85° for 3 hr. Water was added, and the organic layer was separated and distilled from phosphoric anhydride, to give *nonafluoro*-1-*trifluoromethyl*cyclo*hexene* (78%), b. p. 75° (Found: C, 26·8%; *M*, 310. C_7F_{12} requires C, 26·9%; *M*, 312).

(*c*) Nonafluoro-1-trifluoromethyl*cyclo*hexene (1·2 g.), potassium permanganate (4 g.), and water (15 ml.) were heated and shaken at 80° (15 hr.) in a sealed tube. Removal of the excess of permanganate with sulphur dioxide and ether-extraction in the usual way (see Part II, *loc. cit.*), followed by distillation of the dried (Na_2SO_4) ethereal extracts, gave a residual white solid which was dried over phosphoric anhydride. A portion of the solid had m. p. 133° after sublimation *in vacuo*. The rest of the solid was exactly neutralised by aqueous sodium hydroxide, and the aqueous solution was freeze-dried to give disodium perfluoroadipate (75% total yield), identified by means of its infrared spectrum.

(*d*) 1-*H*-Decafluoro-2-trifluoromethyl*cyclo*hexane (2·1 g.) was sealed in a silica tube with water (2 ml.) and a 10% excess of chlorine and irradiated for 48 hr. Distillation of the dried (P_2O_5) organic layer gave 1-*chlorodecafluoro*-2-*trifluoromethyl*cyclo*hexane* (78%), b. p. 103° (Found: C, 22·8%; *M*, 365. C_7ClF_{13} requires C, 22·9%; *M*, 366·5), and unchanged starting material (5%).

The same chloro-compound was produced in 85% yield by reaction of decafluoro-1-iodo-2-trifluoromethyl*cyclo*hexane (1·5 g.) with chlorine (30% excess) in a sealed tube on exposure to ultraviolet light (3 days). The iodo-compound (2·7 g.) and a 20% excess of bromine, kept in the dark (2 days), then irradiated (2 days), gave 1-*bromodecafluoro*-2-*trifluoromethyl*cyclo-*hexane* (78%), b. p. 115° (Found: C, 20·4%; *M*, 407. C_7BrF_{13} requires C, 20·4%; *M*, 411).

(*e*) Nonafluoro-2-trifluoromethyl*cyclo*hexene (1·0 g.) and chlorine (10% excess), strongly irradiated in a 10 ml. silica tube at 80° (4 days), gave **1** : 2-*dichlorononafluoro*-1-*trifluoromethyl*-cyclo*hexane* (65%), micro-b. p. 130° (Found: C, 21·9. $C_7Cl_2F_{12}$ requires C, 21·9%), and unchanged olefin (15%).

Similar reaction with bromine for 7 days gave **1** : 2-*dibromononafluoro*-1-*trifluoromethyl*cyclo-*hexane* (57%), b. p. 160° (Found: C, 17·8. $C_7Br_2F_{12}$ requires C, 17·8%), and recovered olefin (28%).

Reaction of Perfluorobut-2-ene.—(a) *With hydrogen iodide.* The olefin (1·68 g.), iodine (0·5 g.), and hydrogen iodide (1·22 g.) failed to react after being heated at 140° (16 hr.).

(b) *With hydrogen bromide.* There was no reaction between perfluorobut-2-ene (1·12 g.) and hydrogen bromide (0·55 g.) when heated at 175° (16 hr.), 200° (23 hr.), or 280° (47 hr.).

The olefin (1·72 g.) and hydrogen bromide (0·73 g.) in a silica tube were exposed to ultraviolet light for 51 hr.; 84% of the olefin underwent reaction. The free bromine which had been produced was removed by reaction with mercury, and the colourless liquid was distilled,

to give 2-*bromo*-1 : 1 : 1 : 2 : 3 : 4 : 4 : 4-*octafluorobutane* (60% based on olefin used), b. p. 53—54°, n_D^{17} 1·307 (Found : C, 17·3; H, 0·6%; *M*, 278. C_4HBrF_8 requires C, 17·1; H, 0·4%; *M*, 281), and 2 : 3-dibromo-octafluorobutane (40% based on olefin used), b. p. 96°, n_D^{18} 1·354.

(c) *With iodine monochloride.* No reaction occurred at room temperature or at 130° (16 hr.). The olefin (1·93 g.) and iodine monochloride (3·1 g.) were heated at 200° (16 hr.) to give a 70% reaction of the olefin. Distillation gave 2 : 3-dichloro-octafluorobutane (90% based on olefin used), b. p. 60—60·5°, identified by means of its infrared spectrum.

A third experiment with perfluorobut-2-ene (1·87 g.) and iodine monochloride (4·2 g.) at 140° (100 hr.) gave only 2 : 3-dichloro-octafluorobutane (90%) and unchanged olefin (43%).

Examination of the still residues from the above experiments by ultraviolet spectroscopy showed that only traces of an organic iodo-compound were present.

(d) *With bromine or chlorine.* Perfluorobut-2-ene (3·7 g.) and bromine (10% excess), irradiated in a silica tube for 5 days, gave 2 : 3-dibromo-octafluorobutane (75%), b. p. 95—96°, n_D^{20} 1·355, and unchanged olefin (18%). Infrared spectroscopic examination of the dibromide and of the unchanged olefin showed that no isomerisation to perfluorobut-1-ene had occurred.

Perfluorobut-2-ene (2·9 g.) and chlorine (20% excess), irradiated in a silica tube (3 days), gave 2 : 3-dichloro-octafluorobutane (88%), b. p. 62°, identified spectroscopically, and unchanged olefin, shown to be spectroscopically free from perfluorobut-1-ene.

(e) *With trifluoroiodomethane.* The butene (2·6 g.) and trifluoroiodomethane (5·1 g.), on exposure to ultraviolet radiation in a silica tube (14 days), gave unchanged olefin (23%) and *octafluoro-2-iodo-3-trifluoromethylbutane* (79%), b. p. 85—86·5° (isoteniscope) (Found : C, 15·4%; *M*, 395. C_5IF_{11} requires C, 15·2%; *M*, 396).

*Reaction of Perfluoro*cyclo*butene.*—(a) *With iodine monochloride.* Perfluoro*cyclo*butene (2·62 g.) and iodine monochloride (5·5 g.) were heated at 140° (2 days), then 170° (3 days), to give unchanged olefin (1·73 g.), 1-*chlorohexafluoro*-2-*iodo*cyclo*butane* (0·95 g.), b. p. 99—100°, n_D^{15} 1·4059 (Found : C, 14·6. C_4ClIF_6 requires C, 14·8%), and 1 : 2-dichlorohexafluoro*cyclo*butane (0·30 g.), b. p. 59°.

In a second experiment the olefin (8·7 g.) and iodine monochloride (18 g.) were heated at 180° (1 day), to give unchanged olefin (2·7 g.), 1-chlorohexafluoro-2-iodo*cyclo*butane (77% based on olefin used), and 1 : 2-dichlorohexafluoro*cyclo*butane (10%). Ultraviolet spectrum of 1-chlorohexafluoro-2-iodo*cyclo*butane in light petroleum : $\lambda_{max.}$ 270 (ε 300); $\lambda_{min.}$ 223 (ε 45).

(b) *With hydrogen bromide.* No reaction occurred when perfluoro*cyclo*butene and hydrogen bromide were heated at 180° (6 days) or at 220° (4 days).

The olefin (3·8 g.) and hydrogen bromide (2·5 g.), irradiated for 3 days, gave 1-bromo-1 : 2 : 2 : 3 : 3 : 4-hexafluoro*cyclo*butane (33% based on olefin used), b. p. 96°, n_D^{20} 1·389 (Found : C, 19·8%; *M*, 243. Calc. for C_4HBrF_6 : C, 19·8%; *M*, 243), 1 : 2-dibromohexafluoro*cyclo*butane (49% based on olefin used), b. p. 62° (Found : C, 14·9%; *M*, 318. Calc. for $C_4Br_2F_6$: C, 15·0%; *M*, 322), and unchanged olefin (35%). The identity of the recovered olefin was confirmed by spectroscopic examination. Park, Sharrah, and Lacher (*J. Amer. Chem. Soc.*, 1949, **71**, 2339) report b. p. 56°/632 mm. for the bromohexafluoro*cyclo*butane.

(c) *With hydrogen iodide.* See Haszeldine and Osborne (*J.*, 1955, 3880).

(d) *With chlorine or bromine.* Perfluoro*cyclo*butene (2·8 g.) and a 10% excess of chlorine, on exposure to ultraviolet light (1 day), gave 1 : 2-dichlorohexafluoro*cyclo*butane (71%) and unchanged olefin (21%).

Perfluoro*cyclo*butene (3·1 g.) and bromine (10% excess), similarly treated, gave 1 : 2-dibromohexafluoro*cyclo*butane (65%) and unchanged olefin (24%). Infrared spectroscopic examination of the recovered olefin showed it to be identical with the starting material.

(e) *With trifluoroiodomethane.* The olefin (3·6 g.) and trifluoroiodomethane (100% excess) in a 50 ml. silica tube, exposed to ultraviolet light (25 days), gave unchanged olefin (30%) and *hexafluoro*-1-*iodo*-2-*trifluoromethyl*cyclo*butane* (67% based on olefin used), b. p. 85—87° (Found : C, 17·0%; *M*, 360. C_5IF_9 requires C, 16·8%; *M*, 358). Spectroscopic examination of the recovered olefin showed it to be identical with the starting product.

*Reactions of Perfluoro*cyclo-*butanes and -butenes.*—(a) 1-*Chlorohexafluoro*-2-*iodo*cyclo*butane.* The iodo-compound (4·9 g.) in ethyl ether (10 ml.) was added slowly (3 hr.) to a suspension of lithium aluminium hydride (2 g.) in ether (30 ml.) under a reflux condenser, and the mixture refluxed for 2 hr. Dilute sulphuric acid (20 ml.) was added cautiously to the cooled mixture, followed by water. The ethereal layer, combined with two ethereal extracts of the aqueous phase, were dried (P_2O_5), then distilled through a short packed column. The fraction of b. p. 25—29° (mainly 27°) (62%) was transferred to an apparatus for manipulation of volatile compounds and further purified by distillation, to give 1 : 1 : 2 : 2 : 3 : 4-hexafluoro*cyclo*butane

(51%), b. p. 27° (isoteniscope) (Found: C, 29·0; H, 1·1%; *M*, 164. Calc. for $C_4H_2F_6$: C, 29·3; H, 1·2%; *M*, 164). Buxton and Tatlow (*loc. cit.*) report b. p. 26·6—27·0°. There was no unchanged iodo-compound, and perfluoro*cyclo*butene was not detected as a product.

1-Chlorohexafluoro-2-iodo*cyclo*butane (1·0 g.), sealed with chlorine (10% excess) in a 5 ml. tube and irradiated (8 hr.), gave 1 : 2-dichlorohexafluoro*cyclo*butane (95%), b. p. 59—60° (Found: *M*, 233. Calc. for $C_4Cl_2F_6$: *M*, 233), identified by means of its infrared spectrum.

(b) 1-*Bromo*-1 : 2 : 2 : 3 : 3 : 4-*hexafluoro*cyclo*butane*. The bromo-compound (2·3 g.) in ether (2 ml.) was treated with lithium aluminium hydride (1 g.) in ether (12 ml.) under conditions similar to those of (a) above. Distillation of the ethereal extracts gave 1 : 1 : 2 : 2 : 3 : 4-hexafluoro*cyclo*butane (63%) (Found: *M*, 163).

The bromo-compound (1·2 g.) and bromine (30% excess) in a 10 ml. silica tube, exposed to intense ultraviolet radiation (4 days), gave 1 : 2-dibromohexafluoro*cyclo*butane (71%), b. p. 95—96° (Found: *M*, 320. Calc. for $C_4Br_2F_6$: *M*, 322), and unchanged monobromo-compound (15%). The dibromo-compound so produced was readily debrominated by zinc and dioxan in a sealed tube at 80° (3 hr.), to give perfluoro*cyclo*butene (81%), identified spectroscopically.

(c) 1 : 2-*Dibromohexafluoro*cyclo*butane*. The dibromo-compound (2·9 g.) was treated with lithium aluminium hydride as in (b) above, to give 1 : 1 : 2 : 2 : 3 : 4-hexafluoro*cyclo*butane (60%) (Found: *M*, 164). As in (a) and (b) above, loss of product occurred by failure to achieve complete separation from ether on the scale used. Reaction of the ether–hexafluoro*cyclo*butane mixture, b. p. 29—32°, with an excess of boron trifluoride rendered further separation possible, since boron trifluoride forms a complex only with the ether.

(d) 1 : 2-*Dichlorohexafluoro*cyclo*butane*. The dichloride (8·6 g.) in ether (5 ml.) was added (2 hr.) to lithium aluminium hydride (2 g.) in ether (40 ml.). The mixture, treated as in (*a*) above, gave 1 : 2 : 2 : 3 : 3 : 4-hexafluoro*cyclo*butane (74%), b. p. 27° (Found: *M*, 164), and no unchanged chloro-compound.

(e) 1 : 1 : 2 : 2 : 3 : 4-*Hexafluoro*cyclo*butane*. The products obtained from reductions of the type described above were combined, treated with boron trifluoride to remove any traces of ether, then redistilled.

A portion (1·7 g.), chlorine (1·6 g.), and water (1 ml.) in a 10 ml. silica tube were exposed to ultraviolet light (5 days), to give 1 : 2-dichlorohexafluoro*cyclo*butane (87%), b. p. 59° (isoteniscope) (Found: *M*, 234. Calc. for $C_4Cl_2F_6$: *M*, 233).

A second portion (2·9 g.), water (20 ml.), potassium permanganate (2 g.), and potassium hydroxide (2 g.) in a 50 ml. autoclave were shaken and heated (80°) for 8 hr. The filtered solution was treated with sulphur dioxide, acidified with sulphuric acid, and extracted with ether in the usual way. The dried (P_2O_5) ethereal extract was evaporated to dryness and the residual hygroscopic solid neutralised with aqueous sodium hydroxide; freeze-drying gave disodium tetrafluorosuccinate (73%), identified by means of its infrared spectrum.

A third portion (1·8 g.), potassium hydroxide (2 g.), and water (2 ml.) were shaken vigorously in a sealed tube (12 hr.), water (10 ml.) was added, and the volatile products were distilled *in vacuo*, giving 1 : 3 : 3 : 4 : 4-pentafluoro*cyclo*butene (77%), b. p. 25° (isoteniscope) (Found: *M*, 134. Calc. for C_4HF_5: *M*, 134). Buxton and Tatlow (*loc. cit.*) report b. p. 25—26° for this compound.

(f) *Hexafluoro*-1-*iodo*-2-*trifluoromethyl*cyclo*butane*. The iodo-compound (5·9 g.) in dioxan (10 ml.) was added during 2 hr. to a vigorously stirred suspension of lithium aluminium hydride (2 g.) in dioxan (50 ml.). After being stirred for a further hour the mixture was heated to 60° (1 hr.), then cooled. Dilute sulphuric acid (30 ml.) was added slowly, then water (100 ml.), and the volatile products, combined with those which had passed through the reflux condenser and been condensed in a trap cooled by liquid oxygen, were transferred to a vacuum-system. Distillation gave 1-H-*hexafluoro*-2-*trifluoromethyl*cyclo*butane* (79%), b. p. 36° (isoteniscope) (Found: C, 25·6; H, 0·4%; *M*, 231. C_5HF_9 requires C, 25·9; H, 0·4%; *M*, 232).

(g) 1-H-*Hexafluoro*-2-*trifluoromethyl*cyclo*butane*. This compound (3·7 g.) was shaken with powdered potassium hydroxide (4 g.) and water (4 ml.) for 5 hr. Distillation of the volatile products *in vacuo* gave *pentafluoro*-1-*trifluoromethyl*cyclo*butene* (83%), b. p. 24° (isoteniscope) (Found: C, 28·3%; *M*, 212. C_5F_8 requires C, 28·3%; *M*, 212).

Pentafluoro-1-trifluoromethyl*cyclo*butene (1·1 g.), mixed with chlorine (0·5 g.) and exposed to ultraviolet light (24 hr.), gave 1 : 2-*dichloropentafluoro*-1-*trifluoromethyl*cyclo*butane* (91%), b. p. 80° (isoteniscope) (Found: C, 21·1%; *M*, 283. $C_5Cl_2F_8$ requires C, 21·2%; *M*, 283).

Pentafluoro-1-trifluoromethyl*cyclo*butene (2·7 g.), potassium permanganate (2 g.), water (15 ml.), and potassium hydroxide (2·1 g.) were shaken vigorously in an autoclave and heated to 75° (8 hr.). The excess of permanganate was removed, and the acid produced was isolated by ether-extraction in the usual way. The solid remaining after evaporation of the ether was

perfluorosuccinic acid (69%), identified by conversion into its disodium salt; the infrared spectrum of the last compound was compared with that of a known specimen.

Perfluorosuccinic acid was also isolated (61%) by reaction of 1-*H*-hexafluoro-2-trifluoromethyl*cyclo*butane (3·0 g.) with permanganate under the above conditions. Fluoroform was also detected as a reaction product by means of its infrared spectrum.

Pyrolysis of Sodium and Potassium Perfluoropentanoate (cf. *J.*, 1952, 4259).—The acid was prepared from perfluoro-*n*-butyl iodide by reaction with acetylene and oxidation (*J.*, 1950, 3037, 2789; 1953, 1548, 3761) and also by electrolysis of pentanoyl fluoride in anhydrous hydrogen fluoride. The sodium and potassium salts were obtained by exact neutralisation of the acid, followed by freeze-drying.

Anhydrous sodium perfluoropentanoate (3·9 g.) in a platinum cylinder with open ends was placed in a platinum tube closed at one end and connected at the other to a trap cooled in liquid oxygen and thence to a pump. The tube was evacuated to 10 mm. and the closed end was then slowly pushed into a furnace at 270°. Gas was evolved steadily and collected in the trap. After 2 hr. the contents of the trap were transferred to a vacuum-apparatus and purified by distillation, to give carbon dioxide and perfluorobut-1-ene (91%), b. p. 0·3° (isoteniscope) (Found: *M*, 200. Calc. for C_4F_8: *M*, 200). Infrared spectroscopic examination showed the presence of a $-CF{:}CF_2$ bond (absorption at 5·57 μ) (*J.*, 1952, 4423; 4259) and that the product was uncontaminated by perfluorobut-2-ene. The olefin combined readily with bromine, when mixed with it in a sealed tube at 25° (5 hr.), to give 1 : 2-dibromo-octafluorobutane (97%), b. p. 95° (Found: *M*, 358. Calc. for $C_4Br_2F_8$: *M*, 360).

Anhydrous potassium perfluoropentanoate (4·1 g.) was pyrolysed under conditions as near to identical as possible with those used for the sodium salt above. The volatile products were carbon dioxide and a mixture of perfluorobutenes (89%) (Found: *M*, 200. Calc. for C_4F_8: *M*, 200). Infrared spectroscopic examination showed the presence of perfluorobut-2-ene (band at 5·77 μ) and perfluorobut-1-ene (band at 5·57 μ). The mixed olefins were then sealed with successive portions of 0·1 g. of bromine and kept for an hour at 25° before refractionation *in vacuo* to separate the dibromide produced and recover the unchanged olefinic material. The recovered olefinic material was then examined by infrared spectroscopy to follow the extent of removal of perfluorobut-1-ene which, as demonstrated by Brice *et al.* (*loc. cit.*) preferentially reacts with the bromine. Reaction with successive small portions of bromine in this way removed all the perfluorobut-1-ene (43% yield) with removal of a negligible amount of perfluorobut-2-ene which remained unattacked (48% yield). Perfluorobut-2-ene combined with bromine when exposed to ultraviolet light at room temperature (5 days), to give 2 : 3-dibromo-octafluorobutane (75%), b. p. 96° (Found: *M*, 360. Calc. for $C_4Br_2F_8$: *M*, 360). Both dibromo-compounds were reconverted into their respective olefins almost quantitatively by reaction with zinc and ethanol.

A mixture of potassium perfluoropentanoate (2·0 g.) and sodium perfluoropentanoate (2·1 g.) was pyrolysed under the above conditions. Infrared spectroscopic examination of the olefin revealed two double-bond bands. The spectrum was almost identical with that of the mixed perfluorobut-1- and -2-ene obtained as above. The mixture was separated in the same way, to give perfluorobut-2- (47%) and -1-ene (45%).

Perfluorobut-1-ene (1·3 g.) was spectroscopically unchanged after being heated with anhydrous potassium fluoride (1·0 g.) at 270° for 8 hr.

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14. *Studies in Hydrogen-bond Formation. Part III.* The Reactivity of Amines, Amides, and Azo-compounds in Aqueous and Non-aqueous Solutions.*

By F. M. Arshid, C. H. Giles, S. K. Jain, and A. S. A. Hassan.

The method of detecting complex-formation in solution by refractometry and dilectric-constant measurement has been applied to binary systems containing basic and other nitrogen-containing compounds, in aqueous and in non-aqueous solution.

The reactions of some substituted and unsubstituted simple aliphatic amides with a variety of second solutes are tentatively interpreted as indicating that the enol-tautomer of the unsubstituted or *N*-monosubstituted compounds predominates in most non-aqueous solutions, and the keto-form in aqueous solutions.

The behaviour of some sulphonated *o*-hydroxyazo-dyes indicates that their azo-groups do not interact in water with alcoholic groups in a second solute.

Experiments with use of the refractive index method to detect intermolecular and chelate complexes involving a variety of nitrogen-containing compounds are described. As one of our aims was the elucidation of the mechanism by which certain polymers, especially proteins, adsorb organic solutes, including dyes, various amido- and amino-compounds have been used as models of these polymers.

The method and general significance of the results have been fully described in Part II (*J.*, 1955, 67). The specific results of the present tests are shown in the Table and the Figure, and their interpretation is discussed below. Some of the present results, as indicated, have also been obtained by the dielectric-constant method.

Reactivity of the Amides.—In view of the importance of the reactivity of the amide group in adsorption by proteins and certain synthetic materials, *e.g.*, nylon, we have examined a number of binary systems containing amides and diamides, in various solvents.

One of the diamides, *viz.*, diacetamidomethane, probably exists in chelated forms:

and thus behaves as a monoamide, whereas in anilidoacetylglycine (Ph·NH·CO·CH_2·NHAc) and diacetamidohexamine no such stable ring can exist and the pairs of amide groups appear to react independently.

If the complexes detected (see Table) are assumed to result from hydrogen-bonding, the results appear to indicate that: (*a*) the tautomeric equilibrium in solutions of unsubstituted and monosubstituted amides is in favour of the enol form in benzene, carbon tetrachloride, or toluene † (as suggested in Part I, *J.*, 1952, 3799), and the keto-form in water. This tentative hypothesis is supported by adsorption on Nylon and wool of a variety of solutes in aqueous and non-aqueous solutions (Chipalkatti, Giles, and Vallance, *J.*, 1954, 4375); (*b*) The reactivity of the carbonyl group in the keto-form is similar to its reactivity in aldehydes (see Part IV, in the press); (*c*) The reactivity of the nitrogen atom in the primary, secondary, and tertiary amides is similar to its reactivity in the corresponding amines.

The tertiary amides, dimethyl- and diethyl-acetamide react with proton acceptors,

* Parts I and II, *J.*, 1952, 3799; 1955, 67.

† Buswell, Rodebusch, and Roy (*J. Amer. Chem. Soc.*, 1938, **60**, 2444) observed, in infrared spectroscopic studies, that monosubstituted amides, *e.g.*, *N*-ethylacetamide, enolise (and associate) in carbon tetrachloride.

Solute b	Solution: Solvent *	Solution: Total concn. (moles)	Method † (temp.)	Mol. ratio of complex (a : b) ‡
		Amides.—Solute a : *Acetamide.*		
Benzoquinone	T, El	0·04	n 20°	1 : 1
,,	W	0·1	n 20	2 : 1
Ethanol	D	0·2	n 21	(1 : 1)
Hæmatoxylin	Ac	0·3	ε —	(2 : 1)
Phenol	W	0·25	n 22	1 : 1
,,	D	0·2	n 21	1 : 1
Pyridine	W	0·2	n 19	1 : 1
Quinol	W	0·25	n 20	2 : 1
Triethylamine	W	0·2	n 19	(1 : 1)
		Solute a : *N*-n-*Butylpropionamide.*		
Diethylamine	T	0·2	ε, n 20	(1 : 2)
Ethanol	T	0·2	ε, n 20	1 : 1*y*
Urea	El	0·1	n 20	1 : 1
		Solute a : *Diethylacetamide.*		
Azobenzene	T	0·1	n 20	4 : 1
		Solute a : *Dimethylacetamide.*		
Azobenzene	T	0·1	n 14	4 : 1
Benzoquinone	T	0·1	n 14	4 : 1
		Solute a : *Dimethylformamide.*		
Acetone	B	0·25	ε —	*x*
Aniline	B	0·25	ε, n 20	2 : 1
Diethylamine	B	0·25	ε —	1 : 1
Diphenylamine	C	0·05	n 17	*x*
Hæmatoxylin	W	0·05	n 20	4 : 1
Phenol	B	0·25	ε —	1 : 1
,,	W	0·25	n 19, 35	1 : 1
,,	C	0·1	n 22	1 : 1, 1 : 2 §
		Diamides.—Solute a : *Diacetamidomethane.*		
Diethylamine	W	0·1	n 17	*x*
,,	El	0·1	n 17	1 : 1
Phenol	El	0·1	n 21	1 : 1
,,	W	0·1	n 17	1 : 1
Pyridine	W	0·2	n 22	*x*
Triethylamine	W	0·1	*n* 17	*x*
,,	El	0·1	*n* 16·5	1 : 1
		Solute a : *Anilidoacetylglycine.*		
Phenol	El	0·1	n 17	1 : 2
Triethylamine	An	0·05	n 17	*x*
,,	El	0·05	n 21	(1 : 2)
		Solute a : *Diacetamidohexane.*		
n-Pentanol	W	0·1	n 19	(1 : 2)
Phenol	El	0·1	n 21	1 : 2
Triethylamine	El	0·1	n 21	*x*
		Amines.—Solute a : *Aniline.*		
Anisole	B	0·25	ε —	*x*
Diethylamine	W	0·25	n 18	1 : 1
Triethylamine	W	0·25	n 19	(1 : 1)
		Solute a : *Diethylamine.*		
Azobenzene	B	0·25	n 19	1 : 1 *z*
o-Nitrophenol	B	0·25	*n* 18	1 : 1
Phenol	B	0·25	n 19	1 : 1 *z*
,,	D	0·1	n 20	1 : 1, (1 : 2)
,,	T	0·05	*n* 17	1 : 1, (1 : 2)
,,	W	0·25	n 18, 20	1 : 1 *y*
Triethylamine	D	0·2	n 22	*x*
,,	W	0·1	n 17	(*x*)
,,	El	0·1	n 17	*x*

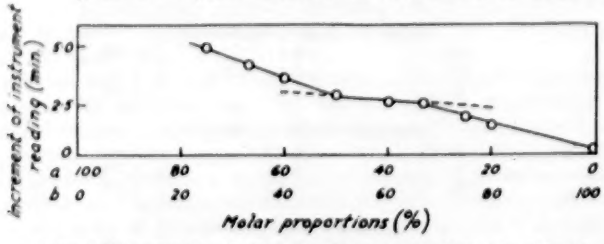
TABLE. (*Continued.*)

Solute b	Solvent *	Solution Total concn. (moles)	Method † (temp.)	Mol. ratio of complex (a : b) ‡
		Solute a : *Triethylamine.*		
Ethanol	W	0·25	n 21	*x*
Resorcinol	T	0·25	ε, n 20	2 : 1
		Azo-compounds.—*Solute* a : $PhNH_2 \rightarrow 2 : 3 : 6\text{-}C_{10}H_5(OH)(SO_3Na)_2$		
Diethylamine	W	0·05	n 20	1 : 2
Ethanol	W	0·05	n 20	*x*
Glycol	W	0·05	n 20	*x*
Phenol	W	0·05	n 20	1 : 1
		Solute a : $PhNH_2 \rightarrow 1\text{-}C_{10}H_7\cdot NH_2$		
Phenol	T	0·1	ε, n 20	(1 : 3, 1 : 4)
		Solute a : $PhNH_2 \rightarrow 3\text{-}C_{10}H_7\cdot NH_2$		
Phenol	T	0·1	ε, n 20	1 : 2
		Solute a : $PhNH_2 \rightarrow 2\text{-}C_{10}H_7\cdot OH$		
Aniline	B	0·25	ε —	2 : 1
Phenol	B	0·25	ε —	1 : 1, (1 : 2)
Quinol	D	0·1	n 20	1 : 1, (2 : 1)
Resorcinol	E	0·25	ε —	2 : 1, 1 : 1
$CCl_2{:}CHCl$	T	0·1	ε, n 20	1 : 2
		Solute a : *Azobenzene.*		
Aniline	B	0·25	n 19	2 : 1 *z*
Benzoquinone	T	0·1	*n* 19	*x*
$PhCH_2\cdot OH$	C	0·1	n 20	1 : 1
Diethylamine	B	0·25	n 19	1 : 1 *z*
Phenol	B	0·25	n 19	1 : 1, 1 : 2 *z*
Triethylamine	D	0·1	n 18	*x*
		Solute a : *Sodium sulphanilate acid→2-naphthol.*		
Glycol	W	0·1	n 20	*x*
Quinol	W	0·1	n 20	2 : 1

* Ac = acetone; An = aniline; B = benzene; C = carbon tetrachloride; D = dioxan; E = diethyl ether; El = ethanol; T = toluene. † ε = dielectric constant; n = refractive index. ‡ Data in parentheses denote uncertain indications. § See Fig.

x No evidence of complex formation. *y* Curves show particularly pronounced change of slope. *z* Results by dielectric constant method reported in Part I.

Relation between refractive index [as instrument reading] and component ratio in (0·1M) binary phenol–dimethylformamide solutions in carbon tetrachloride.



a, Dimethylformamide; *b*, Phenol. Solvent : Carbon tetrachloride.

This system has been re-examined with a refractometer of higher precision and at a different temperature, and a 2 : 1 complex is now evident in addition to the 1 : 1 complex already detected (Part II, Fig. 6). This emphasises the fact discussed in Part II, that evidence of no complex formation is not necessarily conclusive if measurements are made at only one temperature or with only one second solute.

Direct instrument readings are plotted here, since over very small ranges these vary linearly with concentration, as do the n^2 values normally used.

presumably through the hydrogen on the α-carbon atom, which is activated by the adjacent carbonyl group.*

Azo-compounds.—The free nitrogen atom in sulphonated *o*-hydroxyazo-compounds forms complexes with phenol in aqueous solution (cf. Part II), but not apparently with alcohols. Diethylamine appears to react by salt-formation with the sulphonic acid groups.

Trichloroethylene in organic solvents evidently forms a complex by a C–H · · · N bond with the azo-group. This may explain its good solvent power for unsulphonated azo-dyes.

The presence of a chelate ring in aniline→2-naphthylamine is revealed by its complex ratio with phenol, when compared with those of aniline→1-naphthylamine and phenol.

Note on Previous Work.—The present methods bear a close relation to the " method of continuous variations " for the spectrophotometric determination of the molar ratio of organic complexes in solution, apparently first studied by Ostromisslensky (*Ber.*, 1911, **44**, 268), although more fully discussed, both as to principles and implications, independently by Denison (*Trans. Faraday Soc.*, 1912, **8**, 20, 35), and later used for inorganic–inorganic and inorganic–organic complexes by Job and his collaborators [Job, *Compt. rend.*, 1925, **180**, 928, 1108, 1932; 1926, **182**, 1621; 1927, **184**, 204, 1066; 1928, **186**, 1546; 1933, **196**, 181; 1934, **198**, 827; 1935, **200**, 831; *Ann. Chim.* (*France*), 1928, **9**, 113; 1936, **6**, 97; Bernard and Job, *Compt. rend.*, 1930, **190**, 186; Job and Brigando, *ibid.*, 1940, **210**, 438] and by Vosburgh and Cooper (*J. Amer. Chem. Soc.*, 1941, **63**, 437). Spacu and Popper (*Z. phys. Chem.*, 1934, *B*, **25**, 460) also determined refractive index values for binary aqueous solutions of certain inorganic salts by a similar method, and detected complex formation.

Experimental

The technique has been fully described in Parts I and II (*locc. cit.*). For the present refractive-index measurements the apparatus mainly used was the new high-precision Bellingham and Stanley Pulfrich instrument.

Anilidoacetylglycine.—Glycine was acetylated and the product condensed with aniline (Granacher, Schelling, and Schlatter, *Helv. Chim. Acta*, 1925, **8**, 873). It formed colourless flakes (from hot water), m. p. 189°.

Diacetamidohexane, prepared by reaction between hexamethylenediamine and acetic anhydride in the cold, formed colourless needles (from water), m. p. 125°.

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* Kandar (*Bull. Chem. Soc. Japan*, 1950, **23**, 4, 137; through *J. Text. Inst.*, 1951, **42**, *A*, 575; *Chem. Researches, Japan*, 1951, **9**, 133; through *Chem. Abs.*, 1951, **45**, 7610) has proposed an α-keratin model embodying this type of C–H · · · N bond between peptide groups. Anslow (*Discuss. Farady Soc.*, 1950, **9**, 299) has observed C–H · · · N and C–H · · · O absorption components in the ultraviolet spectra of some protein solutions.

15. *The Solvolysis of* 1-*Chloropropan*-2-*ol.*

By I. K. Gregor, N. V. Riggs, and V. R. Stimson.

Solvolysis of 1-chloropropan-2-ol in water produces acid, acetone, and propane-1 : 2-diol simultaneously at comparable first-order specific rates. The glycol yields no carbonyl-containing products in moderately concentrated acid at 97°. Rates of solvolysis of ethylene chlorohydrin have also been determined.

Ethylene chlorohydrin on solvolysis yields only small amounts of acetaldehyde (*ca.* 1%) (Cowan, McCabe, and Warner, *J. Amer. Chem. Soc.*, 1950, **72**, 1194) whereas 1-chloro-2-methylpropan-2-ol gives eventually a quantitative yield of *iso*butyraldehyde by a reaction subsequent to that producing acid (Harvey, Riggs, and Stimson, *J.*, 1955, **3267**). The kinetics and products of the solvolysis of 1-chloropropan-2-ol are now reported.

Rates of solvolysis in water of ethylene chlorohydrin have been determined by Radulescu and Muresanu (*Bul. Soc. stiinte Cluj*, 1932, **7**, 129; *Chem. Abs.*, 1933, **27**, 2085). Further measurements made with this compound (Table 1) agree very well with theirs.

Table 1. *Solvolysis of ethylene chlorohydrin and* 1-*chloropropan*-2-*ol.*

	Ethylene chlorohydrin			1-Chloropropan-2-ol		
Solvent (% v/v)	Temp.	10^3C_0 (mole/l.)	10^6k_1 (sec.$^{-1}$)	Temp.	10^3C_0 (mole/l.)	10^6k_1 (sec.$^{-1}$)
Water	124·9°	2·6	51·0	118·5°	2·72	28·8
	97·2	3·0	3·98	115·8	2·69	22·3
	83·2	2·8	0·95	97·2	2·63	3·23
	83·2	3·0	0·98	97·2	2·78	3·21
60%-EtOH	97·2	3·1	0·88	97·2	2·78	0·53
	97·2	3·4	0·92	—	—	—
80%-EtOH	97·2	3·1	0·38	97·2	2·75	0·16

Experimental

Materials.—1-Chloropropan-2-ol was made by the hydration of allyl chloride (Bancroft, *J. Amer. Chem. Soc.*, 1919, **41**, 426). The product (b. p. 43—46°/18 mm., n_D^{17} 1·4388) was fractionated through an 8″ × 1″ column packed with Fenske helices and fitted with a Whitmore–Lux head, a fraction having b. p. 40·8—41·0°/18 mm., n_D^{19} 1·4381, d_4^{20} 1·1123, being retained (Found : C, 37·8; H, 7·53. Calc. for C_3H_7OCl : C, 38·0; H, 7·46%).

Ethylene chlorohydrin (L. Light and Co.) was distilled; the fraction having b. p. 124°/680 mm. and n_D^{21} 1·4410 on being refractionated as above yielded a sample, b. p. 45·4—45·9°/26 mm., n_D^{21} 1·4411.

Products.—Samples of 1-chloropropan-2-ol (0·2 g.) in water (5 ml.) were heated at 97° in sealed tubes for measured times and cooled. The consumption of periodate during 2 hr. at room temperature in a borax–boric acid buffer was attributed to propane-1 : 2-diol, which was shown to react quantitatively under these conditions. Similar samples were treated with 2 : 4-dinitrophenylhydrazine solution. The resulting precipitate was filtered off, dried, and extracted with benzene. The extract was chromatographed on alumina, and the product (m. p. and mixed m. p. with acetone 2 : 4-dinitrophenylhydrazone 126°) weighed. No other yellow bands were observed on the column.

Samples of propane-1 : 2-diol (b. p. 91·3°/17 mm., n_D^{17} 1·4331; 0·2 g.) were heated at 97° for various times up to 160 hr. in hydrochloric acid of concentrations up to 2N. No carbonyl-containing product was detected with 2 : 4-dinitrophenylhydrazine.

Kinetics.—The solvents were purified, solutions made up, and the kinetics of acid production determined as described by Harvey, Riggs, and Stimson (*loc. cit.*). The specific rate constants for the production of glycol and acetone were calculated from $k_1 = (1/t) \log_e [x_\infty/(x_\infty - x_t)]$ where x_t is the amount of acetone or glycol produced after time t.

Discussion

In water at 97° 1-chloropropan-2-ol yields acid, acetone, and propane-1 : 2-diol simultaneously, the kinetics of production being of the first order in each case and the specific

rate constants nearly equal, *viz.*, $10^6k_1 = 3{\cdot}2$, 2·6, and 3·5 sec.$^{-1}$, respectively. Since steady rate constants for acid production are obtained by calculation from the concentration of 1-chloropropan-2-ol (Table 2), 1·0 mol. of acid is liberated, whereas the ultimate

TABLE 2. *Rate of production of acid in the solvolysis of 1-chloropropan-2-ol.*

Solvent, water. Temp., 118·5°. Concn. of C_3H_7OCl, 13·65 × 10^{-4} mole/bulb. Concn. of $Ba(OH)_2$, 0·01025*N*.

Time (min.)	105	152	196	236	274	302	332	362	382	382
Titre (ml.)	2·23	3·12	3·86	4·45	5·04	5·39	5·69	6·15	6·36	6·42
10^6k_1 (sec.$^{-1}$)	2·90	2·93	2·92	2·88	2·90	2·85	2·82	2·85	2·83	2·87

Mean $k_1 = 2{\cdot}88 \pm 0{\cdot}04 \times 10^{-6}$ sec.$^{-1}$.

yields of acetone and propane-1 : 2-diol are 0·42 and 0·48 mol., respectively, a total of 0·90 mol. The discrepancy may be due to accumulated errors in the methods of estimation or to the formation of other products; in particular, no propaldehyde was detected (cf. Krassuski, *J. Russ. Phys. Chem. Soc.*, 1902, **34**, 287). Further, propane-1 : 2-diol, unlike 2-methylpropane-1 : 2-diol, does not rearrange on prolonged heating with moderately concentrated acid. Wegscheider's test (Table 3) shows that acetone and propane-1 : 2-diol are produced in side reactions.

TABLE 3. *Rates of formation of products in the solvolysis of 1-chloropropan-2-ol in water at 97°.*

Time (hr.)	15	46·5	99·5	189	426(∞)
Acetone (mol.)	0·059	0·15	0·26	0·34	0·42
10^6k_1 (sec.$^{-1}$)	2·8	2·5	2·8	2·5	—
Acetone/HCl (calc.)	0·37	0·36	0·38	0·38	—
Time (hr.)	48	108·5	171	498(∞)	—
Glycol (mol.)	0·22	0·38	0·41	0·48	—
10^6k_1 (sec.$^{-1}$)	3·6	3·9	3·1	—	—
Glycol/HCl (calc.)	0·51	0·53	0·48	—	—

The overall rate of disappearance of 1-chloropropan-2-ol, as measured by the acid produced, falls as ethanol replaces water in the solvent, and to a greater extent than in the solvolyses of ethylene chlorohydrin and 1-chloro-2-methylpropan-2-ol, being twenty times as great in water as in " 80% " ethanol at 97°, whereas the factor is 10 for the last two compounds; the ratios of rates in " 60% " and " 80% " ethanol are 3·3, 2·3, and 2·4 respectively.

The activation energy (29·6 kcal./mole) calculated from the Arrhenius equation is appreciably different from those for ethylene chlorohydrin and 1-chloro-2-methylpropan-2-ol (26·5 and 27·0 kcal./mole respectively), but the results do not show whether the present value can be assigned to a single rate-determining stage or whether it is a composite value for the side reactions. The values of $\log_{10}A$ are 12·1, 10·2, and 11·3 respectively.

The relative rates of solvolysis of ethylene chlorohydrin, 1-chloropropan-2-ol, and 1-chloro-2-methylpropan-2-ol in water at 97° are 1·0 : 0·81 : 5·5. Successive introduction of methyl groups into the β-position of ethylene chlorohydrin does not, therefore, cause progressive changes in the rates or kinetic parameters discussed above. Further, the nature and proportions of the products and the reaction paths by which they are produced differ considerably from case to case.

The microanalysis was carried out by Dr. W. Zimmermann, of C.S.I.R.O., Melbourne.

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16. *Magnetochemistry of the Heaviest Elements. Part IX.* The System* UO_2–ThO_2–O.

By J. K. Dawson and L. E. J. Roberts.

The magnetic susceptibility per uranium atom of partially oxidised samples of urania–thoria solid solutions has been measured at three different urania concentrations. In each case the susceptibility decreased linearly as the average valency of the uranium increased from 4 to 5, more rapidly than in the oxidation of pure urania and at a rate that would have led to zero susceptibility before the uranium reached a valency of 6. A possible explanation is that U(IV) is replaced by U(V) in the initial stages of oxidation of these mixed crystals.

The magnetic properties of fully reduced urania–thoria solid solutions have been investigated by several authors, the general conclusions being that all the solid solutions obeyed the Curie–Weiss law and the susceptibility of the urania at infinite dilution approached the theoretical "spin-only" value for two unpaired electrons (Trzebiatowski and Selwood, *J. Amer. Chem. Soc.*, 1950, **72**, 4504; Dawson and Lister, *J.*, 1952, 5041; Slowinski and Elliott, *Acta Cryst.*, 1952, **5**, 768). Although the Weiss constant decreased approximately linearly with uranium concentration, Slowinski and Elliott found that there was a deviation below about 30% uranium so that the Weiss constant did not fall to zero at infinite dilution.

Anderson, Edgington, Roberts, and Wait (*J.*, 1954, 3324) have recently studied the oxidation of urania–thoria solid solutions. They have shown that oxidation to an average uranium valency as high as 5·5 can take place while the lattice retains its cubic symmetry and the extra oxygen enters interstitial positions in the lattice. There were indications that the type of interaction between uranium and oxygen changed as the uranium valency increased beyond 5·0 and it was felt that magnetic susceptibility measurements on these oxidised materials could give further information on this since it should be possible to detect the difference between paramagnetic U(V) and diamagnetic U(VI) if they replace U(IV) ions as a result of the oxidation.

Experimental

Solid solutions containing 27·9% and 43·1% of urania in thoria were prepared by coprecipitation of ammonium diuranate and thorium hydroxide followed by ignition of the dried precipitate in an alumina crucible at 1200° in a stream of carbon monoxide. A solid solution of 14·8% of urania in thoria was obtained by coprecipitation followed by ignition at 2000° in a vacuum-furnace.

Magnetic susceptibility of oxidised urania–thoria solid solutions.

U	Atomic ratio Th	O	Average U valency	$10^6\chi_M^{20°}$	Susceptibility per U atom *	Weiss constant
0·148	0·852	2	4·00	1·83	3450×10^{-6}	45
			4·68	0·93	1840	31
			4·91	0·62	1280	—
			5·19	0·36	817	30
			5·46	0·26	638	37
0·279	0·721	2	4·00	2·94	2880	35
			4·45	2·14	2130	32
			4·99	1·05	1110	42
			5·37	0·61	667	55
0·431	0·569	2	4·00	4·35	2730	57
			4·32	3·51	2220	—
			5·02	1·47	960	56
			5·20	1·02	680	60

* Calc. after correction for the diamagnetism of ThO_2 (30×10^{-6} per mole) but not for the underlying diamagnetism of the uranium ions.

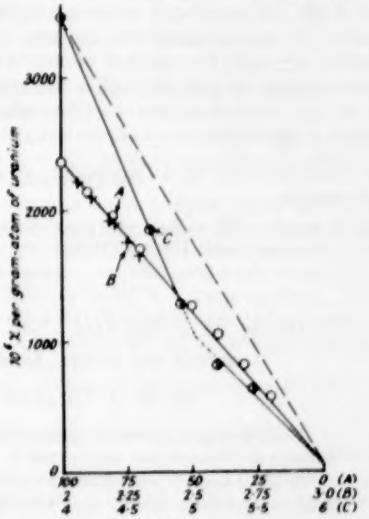
* Part VIII, *J.*, 1954, 3393.

Oxidation of the solid solutions to mean uranium valencies up to 5·0 was carried out by adding known quantities of oxygen gas at 400—600° and annealing for a short time at 800°. Oxidation beyond a mean uranium valency of 5·0 required high pressures of oxygen at 500°. The products were analysed by reducing known weights with carbon monoxide and measuring the carbon dioxide evolved.

The magnetic suceptibilities were measured on the powdered samples by means of the balance described previously (Dawson and Lister, *J.*, 1950, 2177). Observations were made at 90°, 200°, and 300° K; the susceptibilities at 300° K and the variation of the Weiss constant are given in the Table.

Discussion

The magnetic susceptibility of the oxidised solid solutions at three different urania concentrations decreases approximately linearly with increasing oxidation between an average uranium valency of 4 and 5; this is shown in the Figure for the 14·8% urania solid solution. Also plotted are the results of Dawson and Lister (*loc. cit.*) on reduced urania–thoria mixed crystals. The susceptibility in that system also decreased approximately



Scale A, UO_2 (%) *in system*, UO_2–ThO_2 (○).

Scale B, UO_2–O_2 *system*, x *in* UO_x (+).

Scale C. Average uranium valency in UO_2–ThO_2–O_2 *system containing* 14·8% *of urania* (◑).

linearly as the U(IV) ions were diluted by diamagnetic Th(IV) ions over the whole concentration range. Provided that the same type of behaviour can be assumed for the dilution of U(IV) by diamagnetic U(VI), the susceptibility of a urania–thoria solid solution should fall linearly to zero on oxidation to an average uranium valency of 6·0 if U(IV) is being replaced by U(VI) as oxidation proceeds. The observed magnetic susceptibility of all the mixed crystals decreases at a greater rate than this, however, as the average uranium valency increases from 4 to 5·0.

A possible explanation of this behaviour is that in the initial stages of oxidation the oxygen enters the lattice in such a way that the uranium ions change from quadrivalent to quinquevalent, appreciable amounts of sexivalent uranium not being formed until the average uranium valency is greater than 5·0. The additional oxygen is probably doubly ionised or covalently linked to the uranium and does not exist as interstitial free atoms. Unfortunately no magnetic data exist on any other compound containing quinquevalent uranium. The magnetic susceptibility of quadrivalent uranium in dilute solution in the thoria lattice has the spin-only value, however, and if the single electron in U(V) is assumed also to have the spin-only value then the theoretical susceptibility for dilute U(V) in thoria would be less than that of an equal mixture of U(IV) and U(VI). Thus the susceptibility might decrease more rapidly if the quadrivalent uranium is replaced by U(V) than if it is replaced by U(VI) on oxidation.

There is some indication that the susceptibility–temperature relation changes at an average uranium valency of about 5·0, in agreement with the postulate made on the basis of *X*-ray diffraction data by Anderson and his co-workers that the type of interaction between oxygen and uranium changes at about the same point.

Anderson *et al.* (*loc. cit.*) have suggested also that the cell contraction caused by a given quantity of added oxygen per uranium atom is independent of the uranium concentration in the crystal; that is, the mechanism is similar over the range 100% urania to 15% urania-in-thoria. However, the present magnetic behaviour appears to differ from that obtained previously for the urania–oxygen system (Dawson and Lister, *J.*, 1950, 2181). The Figure compares the behaviour of 14·8% urania-in-thoria with that of pure urania on oxidation. Observations on the pure urania system are not valid beyond 30% replacement of U(IV), *i.e.*, $UO_{2\cdot30}$, owing to the appearance of a second phase at that point; nevertheless, over the limited single-phase region it appears that the results follow very closely the theoretical line expected for the replacement of U(IV) by a diamagnetic ion [U(VI)] rather than by paramagnetic U(V). However, the magnetic interaction of interstitial oxygen with the undiluted oxide may differ from that where the oxygen is partially surrounded by quadrivalent thorium ions, and a direct comparison may not be valid.

Finally, although the number of results is rather small, it may be noted that the Weiss constant appears to pass through a minimum at an average uranium valency of about 5, being in this respect similar to the variation of cell constant as deduced from *X*-ray diffraction data (Anderson *et al.*, *loc. cit.*).

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17. *Solutions in Sulphuric Acid. Part XVII.* Cryoscopic Measurements on Some Univalent Metal Sulphates.*

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Earlier cryoscopic measurements on solutions of potassium and ammonium sulphates in sulphuric acid (Part I, Gillespie, Hughes, and Ingold, *J.*, 1950, 2473) have been repeated and new measurements have been made on lithium, sodium, cæsium, silver, and thallous sulphates. It has been shown that osmotic coefficients calculated from the experimental results for all the electrolytes studied may be fitted to an extended form of the Debye–Hückel equation using a value of the dielectric constant of 115 at 10° c. Some information concerning the solvation of the lithium, sodium, potassium, cæsium, and ammonium ions has also been obtained, and the possibility of incomplete dissociation of silver and thallous hydrogen sulphates is discussed.

Because of the apparently close agreement between the experimental freezing-point depressions obtained for a wide variety of solutes, both organic and inorganic, and the corresponding ideal freezing-point depressions if allowance was made in most cases for some solvation of the formed ions, it was suggested in Part I (*loc. cit.*) that the measurements supported the earlier conclusion by Treffers and Hammett (*J. Amer. Chem. Soc.*, 1937, **59**, 1788) that interionic forces in sulphuric acid are negligibly small. It was further suggested that this could be plausibly accounted for if sulphuric acid had a very high dielectric constant. There are now, however, several reasons why this earlier work needs re-examination and some re-interpretation. First, most of the measurements on which these conclusions were based were made in slightly aqueous sulphuric acid and, as was first pointed out in Part VIII (Gillespie, *J.*, 1950, 2997), the exact interpretation of the results is complicated because of the need to take into account any incompleteness in the repression

* Part XVI, *J.*, 1954, 1851.

of the self-ionisation of the solvent, the possibility that the ionisation of the water is repressed by the added solute, and the solvation of the ions formed by the ionisation of the water. Secondly, a more accurate value for the cryoscopic constant of 6·12 may be calculated (Part XVI, Gillespie, *J.*, 1954, 1851) from Rubin and Giauque's determination of the heat of fusion of sulphuric acid (*J. Amer. Chem. Soc.*, 1952, **74**, 800). Thirdly, Brand, James, and Rutherford (*J.*, 1953, 2447) have given a value of 110 at 25° c for the static dielectric constant of sulphuric acid extrapolated from dielectric absorption measurements in the frequency range 300—3000 Mc, and this value has been approximately confirmed by Gillespie and White (unpublished measurements) using Furth's "ellipsoid method" (*Z. Physik*, 1924, **22**, 98).

Previous cryoscopic measurements on ammonium and potassium sulphates in 100% sulphuric acid (Part I, *loc. cit.*) have now been repeated and extended to a number of other metal sulphates in order to provide a sufficient body of results, the interpretation of which would be free from the ambiguities resulting from the presence of water, and which could be used to determine how far the earlier conclusions concerning the behaviour of electrolytes in sulphuric acid could still be regarded as valid.

Experimental

The apparatus and general procedure for making the cryoscopic measurements have been described previously (Part I, *loc. cit.*). Freezing points were measured either with a platinum resistance thermometer and a Smith's difference bridge as described in Part I, or with a solid-stem mercury-in-glass thermometer (Part XIV, Gillespie and Leisten, *J.*, 1954, 1) which was periodically calibrated against the platinum resistance thermometer.

The solvent used in all cases was sulphuric acid of maximum freezing point, which was prepared as follows: A dilute oleum was first prepared from "AnalaR" 98% sulphuric acid and sulphur trioxide distilled from 65% oleum. Approximately 1 l. of this acid was then partially frozen in a 2-l. three-necked flask, and the freezing point observed while aqueous acid was added with good stirring until the maximum freezing point had been reached. Each sample of sulphuric acid used in an experiment was then finally adjusted to exactly the maximum freezing point in the freezing-point cell by the addition of small weighed quantities of aqueous acid or oleum, immediately before beginning the experiment.

All the metal sulphates were of "AnalaR" purity and were dried in an oven at 120° and stored in desiccators over phosphoric oxide.

A supercooling correction of $\delta T = 0{\cdot}0125s\theta$, where s is the amount of supercooling and θ the observed freezing-point depression, was applied to all the observed freezing points (Part I, *loc. cit.*). The numerical factor 0·0125, which differs slightly from the value of 0·012 used in the earlier Parts of this series, is based on the value of the heat of fusion of 2560 cal. (Rubin and Giauque, *loc. cit.*).

Results

Because of the large number of freezing points measured the results are not presented in detail but are given in the form of a Table giving the freezing points of the solutions at certain definite concentrations in order to facilitate the comparison of the different electrolytes investigated. These freezing points were obtained from large-scale plots of the experimental results. A smooth curve was drawn through the experimental points for at least three and

Table 1. *Freezing points of solutions of univalent metal sulphates.*

Molality	Na_2SO_4	K_2SO_4	Li_2SO_4	Cs_2SO_4	$(NH_4)_2SO_4$	Tl_2SO_4	Ag_2SO_4
0·00	10·365°	10·365°	10·365°	10·365°	10·365°	10·365°	10·365°
0·01	10·200	10·203	10·203	10·205	10·205	10·208	10·208
0·02	9·985	9·990	9·990	9·995	9·996	10·000	10·002
0·03	9·745	9·757	9·754	9·764	9·770	9·782	9·780
0·04	9·501	9·518	9·518	9·526	9·540	9·553	9·555
0·05	9·251	9·276	9·280	9·286	9·305	9·328	9·326
0·06	8·994	9·027	9·030	9·043	9·068	9·100	9·097
0·07	8·736	8·772	8·780	8·800	8·827	8·867	8·868
0·08	8·472	8·516	8·525	8·558	8·588	8·637	8·638
0·09	8·208	8·261	8·272	8·311	8·348	8·404	8·414
0·10	7·940	8·007	8·026	8·060	8·105	8·170	8·185
0·11	7·670	7·751	7·762	7·805	7·860	—	7·953
0·12	7·397	7·492	7·498	—	7·615	—	—

generally more experiments for each electrolyte in each of which from five to twelve additions of the solute were made. The freezing points obtained in this way for solutions of sodium, potassium, lithium, cæsium, ammonium, thallous, and silver sulphates are given in Table 1.

Discussion

The Freezing Point of Sulphuric Acid.—In Part I (*loc. cit.*) the freezing point of sulphuric acid was given as 10·36° ± 0·01°. Shortly after the publication of that work Gable, Betz, and Maron (*J. Amer. Chem. Soc.*, 1950, **72**, 1445) obtained the value of 10·37°, and this was later confirmed by Kunzler and Giauque (*ibid.*, 1952, **74**, 297) who gave a value of 10·371°. The highest value of the freezing point that we have been able to obtain consistently is 10·365° and the small difference between this value and 10·371° may be attributed to inaccuracies in the calibration of our thermometers and perhaps to slight impurities in our acid. For the purpose of the present discussion, in which we are concerned only with freezing-point depressions, we have adopted 10·365° as the freezing point of sulphuric acid. Occasionally sulphuric acid was used which had a freezing point that was a few thousandths of a degree lower and in such cases all the observed freezing points of solutions in these samples of acid were corrected by adding the difference between the initial freezing-point of the acid and 10·365°. The procedure is justifiable if the impurity in the sulphuric acid causing the freezing-point lowering is neither sulphur trioxide nor water and if it does not react in any way with the added solute. It is probable that any impurity that was present was, in fact, not sulphur trioxide or water since the freezing point was carefully adjusted to as near as possible the maximum value by addition of oleum or aqueous acid. In any case the values of the freezing points given in Table 1 are based only on the experiments in which the initial freezing point of the acid did not differ by more than a few thousandths of a degree from 10·365° and in which duplicate runs after correction to correspond to a maximum freezing point of 10·365° gave agreement to within 0·02° at the highest concentrations.

The Self-dissociation Equilibria in Sulphuric Acid.—The calculation and interpretation of the osmotic coefficients of solutions of electrolytes in sulphuric acid is considerably affected by the fact that sulphuric acid undergoes appreciable self-dissociation, and it is therefore necessary to consider this self-dissociation in some detail. In Part I (*loc. cit.*), Part II (Gillespie, *J.*, 1950, 2493), and Part IV (*idem*, *J.*, 1950, 2516) it was shown that the self-dissociation occurs according to the equations :

$$2H_2SO_4 = H_2O + H_2S_2O_7 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$H_2O + H_2SO_4 = H_3O^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$H_2S_2O_7 + H_2SO_4 = H_3SO_4^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and that there will also be set up the equilibria :

$$2H_2SO_4 = H_3SO_4^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and

$$2H_2SO_4 = H_3O^+ + HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Reaction (4) is simply the autoprotolysis of the solvent, and reaction (5) was termed the ionic self-dehydration. It was assumed as a first approximation that reactions (2) and (3) go essentially to completion and it was shown that the concentrations of the self-dissociation ions are determined by two equilibrium constants

$$K_{ap} = [H_3SO_4^+][HSO_4^-] = 1{\cdot}7 \times 10^{-4} \text{ mole}^2 \text{ kg.}^{-2}$$

$$K_{id} = [H_3O^+][HS_2O_7^-] = 0{\cdot}7 \times 10^{-4} \text{ mole}^2 \text{ kg.}^{-4}$$

The value of the autoprotolysis constant is of particular importance to our present discussion and we have recalculated it using the new value of the cryoscopic constant and the observed freezing-point curves of all the electrolytes investigated except silver and thallous sulphates.

The addition to sulphuric acid of any solute that produces hydrogen sulphate ions will

modify the concentrations of the self-dissociation products, and in so far as the approximation made above is correct it will repress the autoprotolysis leaving the concentration of hydroxonium and hydrogen disulphate ions unchanged. The observed freezing points for solutions of such an electrolyte may be used to obtain a value for the autoprotolysis constant. By assuming a reasonable approximate value for this quantity, the observed freezing-point curve may be corrected to obtain an approximation to the freezing-point curve that would be given by the solute in a hypothetical acid with zero concentration of autoprotolytic ions, and extrapolation of this curve to zero concentration of added solute gives the freezing point (T_0') of this hypothetical acid. From the difference between this freezing point and the observed freezing point of sulphuric acid, the concentration of the autoprotolytic ions and hence an improved value of the autoprotolysis constant K_{ap} may be calculated. The calculations may be repeated until self-consistent values of the freezing point of the hypothetical acid and the autoprotolysis constant are obtained and until the corrected freezing-point curve agrees, apart from small deviations due to non-ideality, with the ideal calculated freezing-point curve referred to the freezing point (T_0') of the hypothetical acid. The value thus obtained was $T_0' = 10{\cdot}515° \pm 0{\cdot}01°$, which differs only slightly from the value $10{\cdot}52° \pm 0{\cdot}02°$ given in Part I. The molality of the autoprotolysis ions is then given by $m_{ap} = \theta/gk_f = 0{\cdot}0250$, where $\theta = 10{\cdot}515 - 10{\cdot}365 = 0{\cdot}150$ and the osmotic coefficient $g = 0{\cdot}981$ (see p. 87). Hence $[H_3SO_4^+] = [HSO_4^-] = 0{\cdot}0125$m, and $K_{ap} = [H_3SO_4^+][HSO_4^-] = 1{\cdot}56 \times 10^{-4}$.

All the self-dissociation equilibria are of course repressed by the addition of either water or sulphur trioxide, and the hypothetical freezing point (T_0'') of completely undissociated sulphuric acid may be obtained from the freezing-point depressions produced by sulphur trioxide and water by extrapolation in a similar manner to that outlined above. It has been shown in Part II that $T_0'' - T_0' = 0{\cdot}100°$ and hence we shall now assign the freezing point of the hypothetical undissociated acid the value of 10·615°, which differs only slightly from the value 10·62 given in Part II. If the freezing-point depression $T_0'' - T_0' = 0{\cdot}100°$ is assumed to be entirely due to the ions H_3O^+ and $HS_2O_7^-$ it corresponds to a value of K_{id} of 7×10^{-5}.

These values of K_{id} and K_{ap} are only approximately correct; the assumptions on which they are based are known not to be exact as it was shown in Part II that water and disulphuric acid are incompletely ionised. It was believed that the errors introduced by the assumptions that water and disulphuric acid are completely ionised were, however, insignificant, and this has now been verified by Gillespie and Solomons (unpublished work) who have calculated the concentrations of all the self-dissociation products in the presence of an electrolyte $MHSO_4$, taking into account the incomplete ionisation of water and disulphuric acid, and have obtained more accurate values of K_{ap} and K_{id}, which are slightly smaller than those given above. Their work shows that the concentrations of un-ionised water and disulphuric acid are in fact not negligible but that, nevertheless, the extrapolation procedure described above to obtain T_0'' is of sufficient accuracy for our present purpose, and that, also, the freezing-point depression produced by the products of the self-dissociation for any concentration of added electrolyte $MHSO_4$, in the range with which we are concerned, may be calculated with sufficient accuracy (*i.e.*, to within 0·002°) by the procedure used previously, based on the approximate values of K_{ap} and K_{id}, ignoring the small concentrations of un-ionised water and disulphuric acid. We shall therefore continue to use this method in the present paper.

The Calculation of Osmotic Coefficients.—The equation relating the freezing-point depression θ to the molality m_2 of the solute may be obtained by a slight modification of equation 7 of Part XVI and is

$$\theta/m_2 = g\nu_2 k_f\left\{1 - \left(\frac{1}{T_0} - \frac{\Delta C_p}{2\Delta H_0'}\right)\theta\right\}\left\{1 + \frac{(2s_2 - \nu_2)m_2}{2m_1}\right\} \quad . \quad . \quad . \quad (1)$$

where ν_2 is the number of moles of ions formed from one mole of the solute, k_f is the cryoscopic constant, T_0 is the freezing point of the pure solvent, ΔC_p is the difference between the heat capacities of the solid and liquid solvent, m_1 is the molality of the solvent,

s_2 is the total number of moles of the solvent required to react with and solvate the ions formed by one mole of the solute, and g is the rational osmotic coefficient of the solvent.

The factor $(1/T_0) - (\Delta C_p/2\Delta H_0')$ may be computed to be 0·00195 deg.$^{-1}$ from the following values: $\Delta H_0' = 2560$ cal. mole^{-1} (Rubin and Giauque, *loc. cit.*), $T_0 = 10·37° = 283·5°$ K (Kunzler and Giauque, *loc. cit.*), and $\Delta C_p = 8·7$ cal. mole^{-1} deg.$^{-1}$ (Rubin and Giauque, *loc. cit.*). The value of k_f has been given as 6·12 in Part XVI (*loc. cit.*). Hence we may write for any solute

$$\theta/m_2 = 6·12\nu_2 g'(1 - 0·001950)\left\{1 + \frac{(2s_2 - \nu_2)}{2m_1} m_2\right\} \quad . \quad . \quad . \quad . \quad (2)$$

where we now denote the osmotic coefficient by g' to indicate that it is calculated on the basis of solvated ions. We shall henceforth use the unprimed symbol g for the osmotic coefficient calculated on the assumption that the ions are not solvated.

It is convenient for our present discussion to divide s_2 into two parts, namely, the number of moles of solvent s_2' that react with one mole of the added solute and the number of moles of solvent s_2'' that are required to solvate the ions and molecules formed in solution from one mole of solute. Thus we have $s_2 = s_2' + s_2''$. For an electrolyte M_2SO_4 ionising according to the equation

$$M_2SO_4 + H_2SO_4 \rightleftharpoons 2M^+ + 2HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (A)$$

we have that $\nu_2 = 4$ and $s_2' = 1$. Hence equation 2 may be written in the form

$$\theta/m_2 = 24·48g'(1 - 0·001950)(1 - m_2/m_1 + s_2''m_2/m_1) \quad . \quad . \quad . \quad (3)$$

We may, if we wish, make ionic solvation part of the general non-ideality and set $s_2'' = 0$; we then have

$$\theta/m_2 = 24·48g(1 - 0·001950)(1 - m_2/m_1) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and for an ideal electrolyte

$$\theta/m_2 = 24·48(1 - 0·001950)(1 - m_2/m_1) \quad . \quad . \quad . \quad . \quad . \quad (5)$$

From equations (4) and (5) we have that

$$g = \theta_{observed}/\theta_{ideal} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The hypothetical completely undissociated acid has been chosen as the standard state in calculating osmotic coefficients. Thus the observed freezing-point depressions have been calculated from the freezing-point (T_0'') of the hypothetical undissociated acid, *viz.*, 10·615°, using the observed freezing points listed in Table 1. These freezing-point depressions are given in Table 2. The freezing-point depression for an ideal electrolyte M_2SO_4 at any concentration is the sum of the depression that it would produce in the completely undissociated solvent and the depression caused by the ions resulting from the self-dissociation at that concentration of added electrolyte. Table 3 shows the calculation of the freezing-point depressions of an ideal electrolyte M_2SO_4. These values were used together with the observed values for the different electrolytes given in Table 2 to calculate

TABLE 2. *Freezing-point depressions produced by univalent metal sulphates.*

Molality	Na_2SO_4	K_2SO_4	Li_2SO_4	Cs_2SO_4	$(NH_4)_2SO_4$	Tl_2SO_4	Ag_2SO_4
0·01	0·415°	0·412°	0·412°	0·410°	0·410°	0·407°	0·407°
0·02	0·630	0·625	0·626	0·620	0·619	0·615	0·613
0·03	0·870	0·858	0·861	0·851	0·845	0·833	0·835
0·04	1·114	1·097	1·097	1·089	1·075	1·062	1·060
0·05	1·364	1·339	1·335	1·329	1·310	1·287	1·289
0·06	1·621	1·588	1·585	1·572	1·547	1·515	1·518
0·07	1·879	1·843	1·835	1·815	1·788	1·748	1·747
0·08	2·143	2·099	2·090	2·057	2·027	1·978	1·977
0·09	2·407	2·354	2·345	2·304	2·267	2·211	2·201
0·10	2·675	2·608	2·595	2·555	2·510	2·445	2·430
0·11	2·945	2·864	2·853	2·810	2·755	—	2·662
0·12	3·218	3·123	3·117	—	3·000	—	—

TABLE 3. *Freezing-point depressions produced by an ideal electrolyte* M_2SO_4.

Molality	θ * (°c)	δ_1 † (°c)	δ_2 ‡ (°c)	θ_{ideal} $(\theta + \delta_1 + \delta_2)$ (°c)	Molality	θ * (°c)	δ_1 † (°c)	δ_2 ‡ (°c)	θ_{ideal} $(\theta + \delta_1 + \delta_2)$ (°c)
0·01	0·244	0·075	0·100	0·419	0·08	1·937	0·012	0·100	2·049
0·02	0·488	0·044	,,	0·632	0·09	2·176	0·011	,,	2·287
0·03	0·732	0·032	,,	0·864	0·10	2·415	0·010	,,	2·525
0·04	0·974	0·024	,,	1·098	0·11	2·653	0·009	,,	2·762
0·05	1·216	0·019	,,	1·335	0·12	2·890	0·008	,,	2·998
0·06	1·457	0·016	,,	1·573	0·13	3·126	0·007	,,	3·233
0·07	1·697	0·014	,,	1·811	0·14	3·362	0·007	,,	3·469

* Calc. by means of eqn. (5) for an ideal electrolyte in the hypothetical undissociated solvent.
† Freezing-point depression caused by the ions remaining from the autoprotolysis calculated from $K_{ap} = 1{\cdot}56 \times 10^{-4}$ and eqn. (5).
‡ Freezing-point depression caused by the constant concentration of ions resulting from the ionic self-dehydration.

TABLE 4. *Osmotic coefficients of solutions of univalent metal sulphates.*

Molality	Na_2SO_4	K_2SO_4	Li_2SO_4	Cs_2SO_4	$(NH_4)_2SO_4$	Tl_2SO_4	Ag_2SO_4
0·01	0·990	0·983	0·983	0·979	0·979	0·971	0·972
0·02	0·997	0·989	0·989	0·981	0·980	0·973	0·970
0·03	1·007	0·993	0·996	0·985	0·978	0·964	0·969
0·04	1·014	0·999	0·999	0·992	0·979	0·967	0·967
0·05	1·023	1·001	1·000	0·995	0·981	0·964	0·965
0·06	1·031	1·010	1·008	0·999	0·983	0·963	0·965
0·07	1·038	1·017	1·014	1·002	0·987	0·965	0·964
0·08	1·046	1·024	1·020	1·004	0·990	0·966	0·965
0·09	1·054	1·029	1·024	1·007	0·991	0·967	0·962
0·10	1·059	1·034	1·028	1·012	0·994	0·968	0·962
0·11	1·066	1·037	1·033	1·018	0·997	—	0·964
0·12	1·073	1·042	1·040	—	1·000	—	—

osmotic coefficients by means of equation (6). The osmotic coefficients thus obtained are listed in Table 4. These osmotic coefficients are therefore values for solutions of the various electrolytes containing also small concentrations of residual self-dissociation ions. The concentrations of the self-dissociation ions are relatively small except at the lowest concentrations of added electrolyte. Thus the depression produced by the self-dissociation ions amounts to 12% of the total depression in a 0·03-molal solution of M_2SO_4, and 4% in a 0·1-molal solution.

The self-dissociation of sulphuric acid gives rise to another slight complication in the interpretation of the osmotic coefficients. The experimental value of the heat of fusion from which the cryoscopic constant has been calculated includes the heat of self-dissociation, and therefore this value of the cryoscopic constant will not be exactly equal to the true value which relates to the hypothetical undissociated acid as the standard state (Wyatt, *J.*, 1953, 1175). Hence osmotic coefficients calculated on the basis of our cryoscopic constant will include a factor equal to the ratio of the true cryoscopic constant to our value. Fortunately it was shown in Part XVI that the contribution of the heat of autoprotolysis to the heat of fusion is probably only approximately 4 cal., which is of the same order of magnitude as the experimental error in the heat of fusion (±3 cal.), and is too small to be detected in our experiments.

Comparison with the Debye–Hückel Theory.—The rational osmotic coefficient g of the solvent is given, according to the Debye–Hückel theory, by the equation

$$g = 1 - \frac{2{\cdot}303}{3} A|z_1 z_2| I^{\frac{1}{2}} \sigma(x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where $x = BaI^{\frac{1}{2}}$ (a is the distance of closest approach of the anion and cation in Ångström units).

$$\sigma(x) = \frac{3}{x^3}\left[(1 + x) - 2\ln(1 + x) - \frac{1}{1 + x}\right],$$

$$A = \left(\frac{2\pi N}{1000}\right)^{\frac{1}{2}} \frac{e^3}{2{\cdot}303(\varepsilon kT)^{\frac{3}{2}}} \qquad 10^8 B = \left(\frac{8\pi Ne^2}{1000\varepsilon kT}\right)^{\frac{1}{2}}$$

I is the ionic strength $= \frac{1}{2}\Sigma c z_i^2$ (c_i is the molar concentration of the ion i and z_i its valency), z_1 and z_2 are the valencies of the cations and anions respectively, and ε is the dielectric constant of the solvent (see, *e.g.*, Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1954, p. 233).

Now we have approximately that $c = m\rho_0$, where ρ_0 is the density of the pure solvent and for an electrolyte M_2SO_4 [cf. eqn. (*A*)], $z_1 = z_2 = 1$ and $I = 2m\rho_0$.

Hence :

$$g = 1 - A'(2m)^{\frac{1}{2}}\sigma(x') \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where $x' = B'\mathring{a}(2m)^{\frac{1}{2}}$

$$A' = \left(\frac{2\pi\rho N_0}{9000}\right)^{\frac{1}{2}}\left(\frac{e^2}{\varepsilon kT}\right)^{\frac{3}{2}} = 0{\cdot}321$$

and

$$B' = \left(\frac{8\pi Ne^2}{1000\varepsilon kT}\right)^{\frac{1}{2}} = 0{\cdot}376$$

taking $\rho_0 = 1{\cdot}827$ (Part XI, Gillespie and Wasif, *J.*, 1953, 215) and $\varepsilon = 115$.
Therefore

$$g = 1 - 0{\cdot}321(2m)^{\frac{1}{2}}\sigma\{0{\cdot}376\mathring{a}(2m)^{\frac{1}{2}}\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

If we set $\mathring{a} = 0$ we obtain the Debye–Hückel limiting law for an electrolyte M_2SO_4 in sulphuric acid :

$$g = 1 - 0{\cdot}321(2m)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The value of the dielectric constant of sulphuric acid at 10° C is unfortunately rather uncertain. Brand, James, and Rutherford (*loc. cit.*) obtained the value of 110 at 20° and suggested the value of 115 at 10°. Gillespie and White (*loc. cit.*) obtained limiting values of 98 and 121 at ~20°, and of 108 and 135 at ~10°. The choice of 115 at 10° therefore seems reasonable, at least as a preliminary value.

We shall find it convenient to express concentrations in terms of the molal ionic strength $\mu = \frac{1}{2}\Sigma m_i z_i^2$, and equations (9) and (10) may then be written :

$$g = 1 - 0{\cdot}321\ \mu^{\frac{1}{2}}\sigma(0{\cdot}376\mathring{a}\mu^{\frac{1}{2}}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

and

$$g = 1 - 0{\cdot}321\mu^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

In the Figure, the osmotic coefficients for the electrolytes lithium, sodium, potassium, cæsium, ammonium, thallous, and silver sulphates, have been plotted against $\mu^{\frac{1}{2}}$, where $\mu = 2m + m_{ap} + m_{id}$. It may be noted that it is not possible to obtain a solution in sulphuric acid having $\mu < m_{ap} + m_{id} = 0{\cdot}0125 + 0{\cdot}0083 = 0{\cdot}0208$ or $\mu^{\frac{1}{2}} < 0{\cdot}1442$. This ionic strength is indicated by the vertical line in the Figure. It may also be noted that the curves for all the electrolytes in the figure must extrapolate to the value $g = 0{\cdot}981$ at $\mu^{\frac{1}{2}} = 0{\cdot}1442$, since this is the value chosen for the osmotic coefficient of pure sulphuric acid, *i.e.*, sulphuric acid containing the products of its self-dissociation (see p. 87).

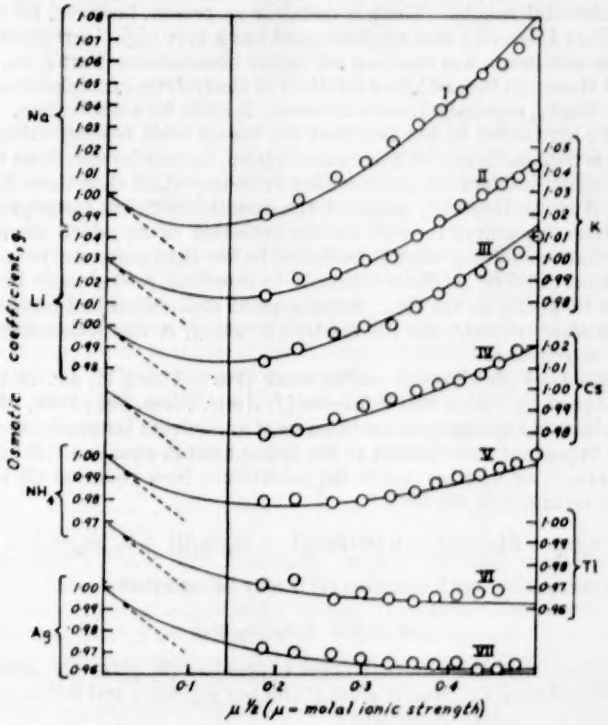
It is found that the osmotic coefficients for sodium, potassium, lithium, cæsium, and ammonium sulphates are greater than predicted by equation (11) for any reasonable value of $\mathring{a}$, and they increase more rapidly with increasing concentration at high concentrations than is consistent with an equation of this form. This type of behaviour is generally attributed, particularly in aqueous solutions, to short-range forces, especially between the ions and the solvent, becoming of comparable importance to the long-range interionic forces that are considered by the Debye–Hückel theory. It has been common practice to allow for the effect of these short-range forces by adding an empirical linear term to the Debye–Hückel expression. If we do this for sulphuric acid we may write :

$$g = 1 - 0{\cdot}321\mu^{\frac{1}{2}}\sigma(0{\cdot}376\mathring{a}\mu^{\frac{1}{2}}) + b\mu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

where b is an empirical constant. It may be seen from the Figure that this equation will fit the observed osmotic coefficients of sodium, lithium, potassium, cæsium, and ammonium

sulphates with $d = 10$ and with values of $b = 0{\cdot}45$, $0{\cdot}3$, $0{\cdot}3$, $0{\cdot}2$, and $0{\cdot}1$ respectively. These values have been chosen so as to give reasonably good agreement between the calculated curves and the experimental results, but they are not necessarily the best possible values that could have been chosen, as it was not considered that the accuracy of the present results was sufficient to warrant an attempt to obtain such values. Only very approximate agreement between these calculated curves and the experimental results is to be expected at the lowest concentrations investigated, partly because the experimental

Comparison of experimental osmotic coefficients with those predicted by equation (13).



○ Experimental values.
– – – – Limiting Debye–Hückel slope (eqn. 12).
——— Calc. from eqn. (13) with the values of the parameters d and b given below.

		d	b			d	b
I	$NaHSO_4$	10	0·45	V	$NH_4{\cdot}HSO_4$	10	0·1
II	$KHSO_4$	10	0·3	VI	$TlHSO_4$	8	0
III	$LiHSO_4$	10	0·3	VII	$AgHSO_4$	8	0
IV	$CsHSO_4$	10	0·2				

error of the measurement of the freezing-point depression increases at low concentrations, and partly because the curves are calculated for a single electrolyte, whereas at low concentrations the self-dissociation products make an appreciable contribution to the total ionic strength. As pointed out earlier, the observed osmotic coefficients for all the electrolytes must extrapolate to the value 0·981 at $\mu^{\frac{1}{2}} = 0{\cdot}1442$, which is the value that was assigned to the osmotic coefficient of pure sulphuric acid. This value was chosen as the mean of the osmotic coefficients at $\mu^{\frac{1}{2}} = 0{\cdot}1442$ of 0·978 and 0·984, calculated for the values $d = 10$ and $b = 0{\cdot}1$ and 0·4 respectively.

The agreement between the calculated curves and the experimental results enables us

to conclude that they are not inconsistent with the value of 115 for the static dielectric constant of sulphuric acid, and therefore they lend a certain support to this value. The same conclusion has been reached by Brand, James, and Rutherford (*loc. cit.*), who showed that our earlier results on the freezing points of solutions of potassium and ammonium sulphates and nitric acid in sulphuric acid containing a little water could be fitted approximately by a simplified form of equation (13) due to Guggenheim (*Phil. Mag.*, 1935, **19**, 588) in which dB' is arbitrarily set equal to unity. It must be realised, however, that a change of as much as 10% in the above value of the dielectric constant would produce an effect on the calculated curves that would only be just sufficient to make them inconsistent with our experimental results. There is certainly no reason, however, for thinking as we did formerly (Part I, *loc. cit.*) that sulphuric acid has a very high " ferroelectric " dielectric constant. This conclusion was based on our earlier observations (Part I, *loc. cit.*) and those of Treffers and Hammett (*loc. cit.*) that solutions of electrolytes in sulphuric acid apparently behave almost ideally, especially if some allowance is made for ion solvation. The apparent ideality may be attributed to the fact that the lowest ionic concentration obtainable in sulphuric acid is 0·02 molal and at this concentration, as may be seen from the Figure, the effects of ion–solvent interactions are becoming more important than those due to interionic forces. Thus, if as was implicitly assumed, the osmotic coefficient for sulphuric acid in the pure acid is taken as unity, then at no concentration of an added electrolyte such as potassium sulphate would the osmotic coefficient be less than unity and hence no deviations from ideality that could be attributed directly to interionic forces would be observed. In the single case in which, at the time, freezing-point depressions had been obtained which were less than ideal, namely, for the electrolyte water, it was reasonably assumed that ionisation was incomplete.

Ionic Solvation.—Following our earlier work (Parts I and II, *loc. cit.*) and the very successful treatment by Stokes and Robinson (*J. Amer. Chem. Soc.*, 1948, **70**, 1870) of ionic activity coefficients in aqueous solution in terms of ion–solvent interactions we may suppose that the most important contribution to the linear term in equation (13) comes from ion–solvent interactions, or in other words ion solvation. Now equation (3) may be written (with sufficient accuracy) in the form

$$\theta/m_2 = 24{\cdot}48g'(1 - 0{\cdot}001959)(1 - m_2/m_1)(1 + s_2''m_2/m_1) \quad . \quad . \quad . \quad (14)$$

from which by comparison with equation (4) it may be seen that

$$g = g'(1 + s_2''m_2/m_1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

Now if we assume that the Debye–Hückel expression (9) gives the osmotic coefficient referred to solvated ions, *i.e.*, that it gives g' and not g (Stokes and Robinson, *loc. cit.*), then we may write for the osmotic coefficient g

$$g = \{1 - 0{\cdot}321\mu^{\frac{1}{2}}\sigma(0{\cdot}376\dot{d}\mu^{\frac{1}{2}})\}(1 + s_2''m_2/m_1) \quad . \quad . \quad . \quad . \quad (16)$$

or, more simply, and to a sufficient approximation

$$g = 1 - 0{\cdot}321\mu^{\frac{1}{2}}\sigma(0{\cdot}376\dot{d}\mu^{\frac{1}{2}}) + s_2''m_2/m_1 \quad . \quad . \quad . \quad . \quad . \quad (17)$$

from which, by comparison with equation (13), we see that $b\mu = s_2''m_2/m_1$; and, since $m_1 = 10{\cdot}20$ and at the higher concentrations $\mu \sim 2m$, $2b = s_2''/10{\cdot}20$, and the value of $b = 0{\cdot}1$, 0·2, 0·3, and 0·45 correspond to total solvation numbers of 2, 4, 6, and 9 respectively. Then if we make the assumption that the hydrogen sulphate ion is not solvated (Part XI, *loc. cit.*) and remember that each mole of metal sulphate produces two moles of cations, we obtain approximate solvation numbers of 1, 2, 3, 3, and 4·5 for the ammonium, cæsium, lithium, potassium, and sodium ions respectively.

The value of the distance of closest approach $\dot{d}$ obtained for electrolytes in aqueous solution is generally between 3 and 5 Å, but the value of $\dot{d} = 10$ that we have obtained is reasonable as it is to a good approximation equal to the calculated values for the various electrolytes if their cations each have one complete solvation shell. We may calculate

from the molal volume of sulphuric acid of 54 c.c. (Part XI, *loc. cit.*) that the mean radius of a sulphuric acid molecule is 2·9 Å. We may to a good approximation take this value also for the mean radius of the hydrogen sulphate ion. If r^+ is the radius of the cation, r^- the radius of the hydrogen sulphate ion, and d the diameter of a sulphuric acid molecule, then the distance of closest approach of a hydrogen sulphate ion and a cation with one complete solvation layer is then given by $\mathring{a} = r^+ + r^- + d$. Values of the distance of closest approach calculated in this way are given in the annexed Table. It may be seen that the calculated values of $\mathring{a}$ are all of the order of 10 Å.

Electrolyte	r^+ (Å)	r^- (Å)	d (Å)	$\mathring{a} = (r^+ + r^- + d)$ (Å)
$LiHSO_4$	0·60	2·90	5·80	9·3
$NaHSO_4$	0·95	,,	,,	9·7
$KHSO_4$	1·33	,,	,,	10·0
NH_4HSO_4	1·48	,,	,,	10·2
$CsHSO_4$	1·69	,,	,,	10·4

The order of increasing osmotic coefficients at any given concentration, and hence of ionic solvation, is $NH_4^+ < Cs^+ < K^+ \sim Li^+ < Na^+$, which is the order to be expected from the size of the ions, except for the anomalous position of lithium. This order of increasing solvation is the same as the order found by viscosity and density measurements in sulphuric acid (Part XI, *loc. cit.*), except that from these results the solvation number of lithium seemed to be closer to that of sodium than to that of potassium. It is interesting to note that the radius ratio of the lithium ion and a sulphuric acid molecule is such that the co-ordination number of lithium is only three. This may account for the fact that its solvation number is approximately three whereas because of its smaller size and hence more intense electric field (compared with that of sodium) it would be expected to have a larger solvation number than sodium. The co-ordination numbers, approximate solvation numbers, and radius ratios for the various cations are given in the following Table :

Cation	Solvation no.	Co-ordination no.	$r^+/r_{H_2SO_4}$
Li^+	3	3	0·207
Na^+	4·5	4	0·327
K^+	3	6	0·458
Cs^+	2	6	0·583
NH_4^+	1	6	0·510

Thus it appears that Li^+ and Na^+ both have complete solvation shells but that those of K^+, Cs^+, and NH_4^+ are incomplete.

Incomplete Dissociation of Silver and Thallous Sulphates.—The results obtained with silver and thallous sulphates are of special interest in that the osmotic coefficients of their solutions decrease with increasing concentration over the whole range studied, and can only be fitted to equation (13) with a value of $\mathring{a}$ less than 10. The results for both thallium and silver can be fitted approximately by taking $\mathring{a} = 8$ and $b = 0$. These values are, however, inconsistent, as for the unsolvated ions we should expect a distance of closest approach for silver and thallium of 4·2 and 4·3 Å respectively. Now there is much evidence that many silver and thallous salts are incompletely dissociated in water, probably because of covalent-bond formation between the anion and the cation, and it does not seem unlikely therefore that the apparently small $\mathring{a}$ value is due to incomplete dissociation. This incomplete dissociation is presumably due to covalent bonding rather than to ion-pair formation, as both the observed distance of closest approach and those calculated for unsolvated ions are greater than the Bjerrum critical distance

$$q = \frac{|z_1 z_2|e^2}{2\varepsilon kT} = 2{\cdot}56 \text{ Å}$$

taking $\varepsilon = 115$, $T = 283{\cdot}5°$ K, and $z_1 = z_2 = 1$. In fact, it appears that because of the high dielectric constant of sulphuric acid and the relatively large size of the hydrogen sulphate ion, it is impossible for any univalent metal hydrogen sulphate to form ion-pairs in sulphuric acid.

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18. *o-Mercapto-azo-compounds. Part VIII.* Preparation and Debenzylation of 2-Benzylthio-2′- and -4′-nitroazobenzene.*

By A. Burawoy, A. Chaudhuri, and C. E. Vellins.

The action of hydrobromic acid and of bromine in glacial acetic acid on 2-benzylthio-2′- and -4′-nitroazobenzene, prepared by condensation in acetic acid of *o*-benzylthioaniline with *o*- and *p*-nitronitrosobenzene respectively, is investigated. The preparation and the reactions of various 2- and 4-nitroazobenzene-2′-sulphenyl derivatives and of the corresponding 2′-sulphinic acids and disulphides are reported.

Debenzylation of 2-benzylthioazobenzene and of 2 : 2′-dibenzylthioazobenzene with bromine and of the former with hydrobromic acid, as well as the properties and reactions of the various compounds formed, have recently been discussed (Parts V, VI, VII *). We have extended this investigation to 2-benzylthio-2′- and -4′-nitroazobenzene (I; X = $S{\cdot}CH_2Ph$) which are obtained by the condensation in acetic acid of *o*-benzylthioaniline with *o*- and *p*-nitronitrosobenzene respectively.

As shown in Part V, 2-benzylthioazobenzene is converted quantitatively by 48% hydrobromic acid in hot acetic acid into azobenzene-2-sulphenyl bromide (~50%) and 3-benzylthiobenzidine dihydrobromide (~50%) according to the general equation (*a*). The reaction is initiated by debenzylation with formation of benzyl bromide and *o*-mercaptoazobenzene which is quickly dehydrogenated to di-(*o*-phenylazophenyl) disulphide, unchanged starting material serving as hydrogen acceptor and being reduced to 2-benzylthiohydrazobenzene. Fission of the disulphide linkage by hydrobromic acid yields azobenzene-2-sulphenyl bromide and *o*-mercaptoazobenzene which re-enters the reaction cycle, whereas 2-benzylthiohydrazobenzene undergoes the benzidine rearrangement. In the presence of azobenzene, the yield of azobenzene-2-sulphenyl bromide is increased, since the starting material is replaced by azobenzene as hydrogen acceptor.

$$\underset{\text{(I)}}{2(\text{or } 4)\text{-}NO_2{\cdot}C_6H_4{\cdot}N{:}N{\cdot}C_6H_4{\cdot}X\text{-}2'} \qquad \underset{\text{(II)}}{[2(\text{or } 4)\text{-}NO_2{\cdot}C_6H_4{\cdot}N{:}N{\cdot}C_6H_4{\cdot}S(2')\text{-}]_2}$$

$$2Ph{\cdot}N{:}N{\cdot}C_6H_4{\cdot}S{\cdot}CH_2Ph + 4HBr \longrightarrow Ph{\cdot}N{:}N{\cdot}C_6H_4{\cdot}SBr + NH_2{\cdot}C_6H_4{\cdot}C_6H_3(NH_2){\cdot}S{\cdot}CH_2Ph,2HBr + Ph{\cdot}CH_2Br \quad . \quad (a)$$

2-Benzylthio-4′-nitroazobenzene behaves similarly, but, in addition to 4-nitroazobenzene-2′-sulphenyl bromide (I; X = SBr), *p*-nitroaniline is isolated in 30% yield, *i.e.*, the 2-benzylthio-4′-nitrohydrazobenzene formed is split by hydrobromic acid in preference to being rearranged (for references to the general tendency of *para*-substituted hydrazobenzenes, under the influence of acids, to undergo disproportionation to aniline derivatives rather than rearrangement see Jacobsen, *Annalen*, 1922, **428**, 76). Again, in the presence of azobenzene the yield of the sulphenyl bromide is considerably increased and *p*-nitroaniline is not detected.

In contrast, heating 2-benzylthio-2′-nitroazobenzene with hydrobromic acid gives only 2-nitroazobenzene-2′-sulphenyl bromide (I; X = SBr). This indicates either that the starting material is unable to serve as a hydrogen acceptor or that its debenzylation is faster than the dehydrogenation of the thiol (I; X = SH) and that the latter is oxidised to di-[*o*-(*o*-nitrophenylazo)phenyl] disulphide (II) which is split by hydrobromic acid as discussed. We have established by independent experiments that both di-[*o*-(*o*-nitrophenylazo)phenyl] disulphide and di-[*o*-(*p*-nitrophenylazo)phenyl] disulphide are quantitatively converted by boiling hydrobromic acid into the corresponding sulphenyl bromides (I; X = SBr).

Both nitro-derivatives (like 2-benzylthioazobenzene and 2 : 2′-dibenzylthioazobenzene) yield almost quantitatively the corresponding stable sulphenyl bromides (I; X = SBr) and the sulphenyl tribromides (I; X = SBr_3) when heated with 1 mol. and with an excess of bromine respectively in acetic acid. 2-Nitroazobenzene-2′-sulphenyl tribromide is rather

* Parts I, V, VI, and VII, *J.*, 1950, 469; 1954, 90, 4481; 1955, 3798.

unstable and cannot be isolated in a pure state, since it quickly dissociates into the sulphenyl bromide and bromine.

Both nitroazobenzene-2′-sulphenyl bromides show many of the reactions characteristic of other known sulphenyl halides. Thus, with dimethylaniline they yield *p*-dimethylaminophenyl *o*-(*o*- and -*p*-nitrophenylazo)phenyl sulphide respectively (I; X = S·C_6H_4·NMe_2-*p*).

Again, on addition of an excess of sodium hydroxide to the suspensions of the bromides in water or aqueous ethanol, deep blue solutions are formed immediately, the colour being due to the presence of the sodium 2- and 4-nitroazobenzene-2′-sulphenate respectively (I; X = SONa). Although the salts could not be isolated, their existence has been established by immediate treatment of the blue alkaline solutions with methyl sulphate, whereupon methyl *o*-(*o*- and -*p*-nitrophenylazo)phenyl sulphoxide respectively (I; X = SMeO) are formed in good yield. [This is similar to the conversion of the blue sodium salts of anthraquinone- and 4-aminoanthraquinone-1-sulphenic acid by methyl sulphate into the corresponding methyl sulphoxides (Fries, *Ber.*, 1912, **45**, 2365; Fries and Schürman, *Ber.*, 1919, **52**, 2170, 2182).] The blue colour disappears slowly, disproportionation taking place with formation of the insoluble di-[*o*-(*o*-nitrophenylazo)phenyl] disulphide and its *p*-nitro-isomer respectively (III) and the soluble sodium 2- and 4-nitroazobenzene-2′-sulphinates respectively (I; X = SO_2Na) which give on acidification the free sulphinic acids.

The *p*-nitro-isomer disproportionates more rapidly. If the stirring of the reaction mixture is continued after the disappearance of the blue colour, the amount of the 4-nitroazobenzene-2′-sulphinic acid increases at the expense of the disulphide and the acid is finally the only product present. The disulphide linkage is split by sodium hydroxide to yield (i) 2-mercapto-4′-nitroazobenzene (I; X = SH) which is quickly reoxidised to the disulphide and (ii) the sulphenic acid (I; X = S·OH) which, again, disproportionates to disulphide and more sulphinic acid (for the similar behaviour of 2-benzylthioazobenzene-2′-sulphenyl bromide towards aqueous sodium hydroxide see Part VII).

The identity of the disulphides has been confirmed by their formation from the corresponding sulphenyl bromides by the action of zinc in boiling benzene solution. The sulphinic acids are also obtained by the treatment of the corresponding sulphenyl tribromides with aqueous sodium hydroxide. Their exclusive formation and the non-appearance of the intermediate blue colour characteristic of the sodium sulphenates confirm the quadrivalency of the sulphur atom in the tribromides. The sulphinic acids have been characterised as nitrobenzyl sulphones (I; X = SO_2·CH_2·C_6H_4·NO_2-*p*) and their structures are confirmed by conversion by hydrobromic acid in acetic acid into the corresponding sulphenyl bromides (for this characteristic reaction of sulphinic acids and references, cf. Parts I, V, and VII).

Both nitroazobenzene-2′-sulphenyl bromides, like azobenzene-2-sulphenyl bromide and 2-benzylthioazobenzene-2′-sulphenyl bromide, but unlike other known sulphenyl bromides, are very stable and water-soluble and are easily converted by double decomposition in water into the cyanide, thiocyanate, chloride, iodide, and perchlorate respectively (I; X = SCN, S·SCN, Cl, I, S·ClO_4).

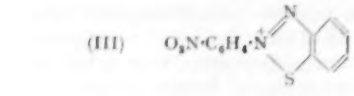
As has been established for the corresponding azobenzene-2-sulphenyl derivatives, these compounds, except for the water-insoluble cyanides, are able to exist as true salts of structure (III). The effect of substituents on the structure and equilibria in different solvents of the azobenzene-2-sulphenyl derivatives is being further investigated by physical methods.

2-Nitroazobenzene-2′-sulphenyl iodide is much less stable to heat than azobenzene-2-sulphenyl iodide and its 4-nitro-derivative. Attempts to crystallise it were unsuccessful, since it dissociates quickly into the disulphide and iodine. 4-Nitroazobenzene-2′-sulphenyl thiocyanate, a reddish-brown crystalline compound after drying in a vacuum, becomes orange-yellow in air with the uptake of 1 mol. of water; the change is reversible and is apparently unaccompanied by a change of the crystal form. The possibility that these two states correspond to the non-ionic and the ionic structure respectively cannot be excluded.

Attempts to reduce the disulphides to the corresponding thiols by ethanolic sodium

sulphide were only partly successful, the reaction being complicated by the presence of the reducible nitro-group. Di-[*o*-(*o*-nitrophenylazo)phenyl] disulphide yields a crude yellow product which could not be purified, but consists mainly of 2-mercapto-2′-nitroazobenzene, since when freshly prepared it is soluble in ethanolic sodium hydroxide and on treatment with methyl sulphate and with benzyl chloride is converted in good yields into 2-methylthio- and 2-benzylthio-2′-nitroazobenzene respectively.

On the other hand, no indication of the formation of 2-mercapto-4′-nitroazobenzene has been obtained on reduction of di-[*o*-(*p*-nitrophenylazo)phenyl] disulphide. Instead, di-[*o*-(*p*-aminophenylazo)phenyl] disulphide (IV) could be isolated, purified through its violet crystalline dihydroperchlorate and further characterised as its *NN*′-dibenzoyl derivative.

(III)  (IV) $(p\text{-}H_2N\cdot C_6H_4\cdot N{:}N\cdot C_6H_4\cdot S\text{-})_2$

Experimental

2-Benzylthio-2′-nitroazobenzene.—*o*-Nitronitrosobenzene (18 g.) in hot acetic acid (250 c.c.) was added to *o*-benzylthioaniline (25 g.) in acetic acid (100 c.c.). The mixture was kept at 50° for 15 min. and at room temperature overnight. The precipitate of almost pure *2-benzylthio-2′-nitroazobenzene* (27 g.) was filtered off and washed with light petroleum. Addition of water to the filtrate yielded a further amount of less pure product (5·5 g.; total yield, 80%). Crystallisation from light petroleum (b. p. 60—80°) or benzene gave orange needles, m. p. 115—116° (Found : C, 65·6; H, 4·4; N, 11·8. $C_{19}H_{15}O_2N_3S$ requires C, 65·3; H, 4·3; N, 12·0%).

2-Benzylthio-4′-nitroazobenzene, similarly prepared, formed orange-red needles, m. p. 167—168°, from benzene (Found : C, 65·2; H, 4·0; N, 11·6%).

2-Nitroazobenzene-2′-sulphenyl Bromide.—2-Benzylthio-2′-nitroazobenzene (10 g.), bromine (4·6 g.), and acetic acid (250 c.c.) were refluxed for 5 min. On cooling, almost pure *2-nitroazobenzene-2′-sulphenyl bromide* separated (9·4 g., 97%). Crystallisation from acetic acid gave yellow needles, m. p. 257—258° (Found : C, 42·1; H, 2·2; N, 12·1. $C_{12}H_8O_2N_3SBr$ requires C, 42·6; H, 2·3; N, 12·4%).

4-Nitroazobenzene-2′-sulphenyl bromide was similarly obtained as yellow needles, m. p. 279—280° (Found : C, 42·8; H, 2·6; N, 12·6%).

Action of Hydrobromic Acid on 2-Benzylthio-4′-nitroazobenzene.—(*a*) 2-Benzylthio-4′-nitroazobenzene (4 g.), acetic acid (120 c.c.), and 48% hydrobromic acid (100 c.c.) were refluxed for 5 min. On cooling, 4-nitroazobenzene-2′-sulphenyl bromide separated (0·8 g.). The filtrate was reduced to a small volume under a vacuum, water was added, and the solution extracted with chloroform from which an additional amount of the sulphenyl bromide was obtained (1·9 g.; total yield, 49%). Crystallisation from acetic acid gave yellow needles, m. p. 279—280° not depressed on admixture with the product described above. The aqueous mother-liquor was made alkaline and extracted with ether, which on concentration yielded *p*-nitroaniline, m. p. and mixed m. p. 146° (0·5 g., 30%).

(*b*) A mixture of 2-benzylthio-4′-nitroazobenzene (2·5 g.), azobenzene (3 g.), acetic acid (80 c.c.), and 48% hydrobromic acid (45 c.c.) was refluxed for 5 min. and poured into water (300 c.c.). The precipitate of almost pure 4-nitroazobenzene-2′-sulphenyl bromide, m. p. 279—280°, was collected (1 g.). Extraction of the filtrate with chloroform yielded an additional amount of the bromide (0·85 g.; total yield, 78%). No *p*-nitroaniline could be isolated.

Action of Hydrobromic Acid on 2-Benzylthio-2′-nitroazobenzene.—This isomer (2 g.), acetic acid (40 c.c.), and 48% hydrobromic acid (60 c.c.) similarly yielded 2-nitroazobenzene-2′-sulphenyl bromide (total yield, 82%). Crystallisation from acetic acid gave yellow needles, m. p. 257—258°, not depressed by the product obtained by the action of bromine. No *o*-nitroaniline was formed.

Action of Zinc on 2-Nitroazobenzene-2′-sulphenyl Bromide.—A solution of 2-nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in benzene (30 c.c.) was refluxed with zinc dust (3 g.) for 15 min. The solution was filtered hot and concentrated. The precipitate of *di-*[o-(*o-nitrophenylazo*)-*phenyl*] *disulphide* was collected (0·25 g., 67%). Crystallisation from benzene gave orange-yellow needles, m. p. 172—173° (Found : C, 56·2; H, 3·6; N, 15·9. $C_{24}H_{16}O_4N_6S_2$ requires C, 55·8; H, 3·1; N, 16·3%).

Action of Zinc on 4-Nitroazobenzene-2′-sulphenyl Bromide.—4-Nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in benzene (200 c.c.) was refluxed with zinc dust (3 g.) for 30 min. After hot filtration and concentration to a small volume, the precipitate of *disulphide* was collected (0·25 g., 67%). It crystallised from benzene as orange needles, m. p. 228—229° (Found: C, 56·1; H, 3·3; S, 12·6. $C_{24}H_{14}O_4N_6S_2$ requires C, 55·8; H, 3·1; S, 12·4%).

Action of Hydrobromic Acid on Di-[o-(o-*nitrophenylazo*)*phenyl*] *Disulphide.*—The disulphide (0·2 g.), acetic acid (15 c.c.), and 48% hydrobromic acid (5 c.c.) were refluxed for 3 min. After cooling and addition of water, the solution was extracted with chloroform from which, on addition of light petroleum, 2-nitroazobenzene-2′-sulphenyl bromide was obtained (0·2 g., 76%). Crystallisation from acetic acid gave yellow needles, m. p. 258°.

The *p*-isomer similarly gave 4-nitroazobenzene-2′-sulphenyl bromide (0·2 g., 76%), crystallising from acetic acid as yellow needles, m. p. 279—280°.

Action of Sodium Hydroxide on 2-Nitroazobenzene-2′-sulphenyl Bromide.—10% Aqueous sodium hydroxide (60 c.c.) was added to a suspension of 2-nitroazobenzene-2′-sulphenyl bromide (3 g.) in water (350 c.c.) and ethanol (100 c.c.). A deep blue solution was formed immediately. After 24 hours' stirring the colour had disappeared and a precipitate of almost pure di-[o-(o-nitrophenyl)azophenyl] disulphide was collected (1·4 g., 92%; m. p. and mixed m. p. 171—173°). On acidification of the filtrate with hydrochloric acid *2-nitroazobenzene-2′-sulphinic acid* separated (0·85 g., 94%). Crystallisation from aqueous ethanol at 50° gave yellow prisms, m. p. 144—145° (Found: C, 49·3; H, 3·4; N, 14·5. $C_{12}H_9O_4N_3S$ requires C, 49·5; H, 3·1; N, 14·4%).

Methyl o-(o-*Nitrophenylazo*)*phenyl Sulphoxide.*—40% Aqueous sodium hydroxide (5 c.c.) was added to a solution of 2-nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in methanol (100 c.c.). The blue solution was shaken immediately with methyl sulphate (3 c.c.) for 30 min.; the blue colour disappeared. After addition of water, the precipitate of *methyl* o-(o-*nitrophenylazo*)*phenyl sulphoxide* was filtered off (0·3 g., 70%). It crystallised from aqueous methanol as orange needles, m. p. 128—129° (Found: C, 54·7; H, 3·8; N, 14·6. $C_{13}H_{11}O_3N_3S$ requires C, 54·0; H, 3·8; N, 14·5%).

Action of Sodium Hydroxide on 4-Nitroazobenzene-2′-sulphenyl Bromide.—10% Aqueous sodium hydroxide (40 c.c.) was added to a suspension of 4-nitroazobenzene-2′-sulphenyl bromide (2 g.) in water (900 c.c.). After 30 minutes' stirring the blue colour, which developed immediately, disappeared and the precipitate of di-[o-(*p*-nitrophenylazo)phenyl] disulphide was filtered off (0·8 g., 78%). It crystallised from benzene as orange needles, m. p. and mixed m. p. 228—229°. On acidification of the filtrate with hydrochloric acid *4-nitroazobenzene-2′-sulphinic acid* separated (0·6 g., 104%). Crystallisation from methanol gave brown-yellow needles, m. p. 133—134° (Found: C, 49·6; H, 3·3; N, 14·3%). The experiment was repeated, but the reaction allowed to proceed for 3 hr.: disulphide (0·55 g., 54%) and sulphinic acid (0·8 g., 137%) were obtained. After 24 hr. only the sulphinic acid could be obtained.

Methyl o-(p-*Nitrophenylazo*)*phenyl Sulphoxide.*—40% Aqueous sodium hydroxide (5 c.c.) was shaken with a solution of 4-nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in methanol (100 c.c.) and methyl sulphate (3 c.c.) for 30 min. After filtration to remove a small amount of disulphide, water was added and the precipitate of almost pure *sulphoxide* collected (0·25 g., 58%). It crystallised from aqueous methanol as orange needles, m. p. 175—176° (Found: C, 54·3; H, 3·7; N, 14·2%).

p-*Dimethylaminophenyl* o-(p-*Nitrophenylazo*)*phenyl Sulphide.*—A solution of 4-nitroazobenzene-2′-sulphenyl bromide (0·6 g.) and dimethylaniline (2 c.c.) in acetic acid (200 c.c.) was refluxed for 1 hr. and subsequently concentrated to a small volume. On addition of water, p-*dimethylaminophenyl* o-(p-*nitrophenylazo*)*phenyl sulphide* separated (0·5 g., 75%). Crystallisation from light petroleum (b. p. 80—100°) gave orange needles, m. p. 187—189° (Found: C, 63·3; H, 4·8; N, 14·7. $C_{20}H_{18}O_2N_4S$ requires C, 63·5; H, 4·8; N, 14·8%).

p-*Dimethylaminophenyl* o-(o-*nitrophenylazo*)*phenyl sulphide*, similarly prepared, crystallised from light petroleum as dark orange needles, m. p. 186—187° (Found: C, 63·6; H, 4·7; N, 15·2%).

4-*Nitrobenzyl* o-(o-*Nitrophenylazo*)*phenyl Sulphone.*—A solution of 4-nitrobenzyl bromide (0·5 g.), 2-nitroazobenzene-2′-sulphinic acid (0·4 g.), and sodium hydroxide (0·08 g.) in ethanol (30 c.c.) was refluxed for 3 hr. On cooling, the *sulphone* separated (0·4 g., 70%). Crystallisation from benzene gave orange needles, m. p. 230—232° (Found: C, 53·0; H, 3·2; N, 13·4. $C_{19}H_{14}O_6N_4S$ requires C, 53·5; H, 3·3; N, 13·2%).

4-*Nitrobenzyl* o-(p-*nitrophenylazo*)*phenyl sulphone* similarly formed an orange-red powder, m. p. 249—250°, from benzene (Found: C, 53·8; H, 3·5; N, 13·3%).

Action of Hydrobromic Acid on 2- and 4-Nitroazobenzene-2′-sulphinic Acid.—(*a*) 2-Nitroazobenzene-2′-sulphinic acid (0·3 g.) in acetic acid (10 c.c.) was refluxed with 48% hydrobromic acid (2 c.c.) for 10 min. On cooling, 2-nitroazobenzene-2′-sulphenyl bromide separated [0·3 g., 86%; yellow needles (from acetic acid), m. p. 257—258°]. (*b*) 4-Nitroazobenzene-2′-sulphinic acid (0·85 g.) in acetic acid (20 c.c.) was refluxed with 48% hydrobromic acid (5 c.c.) for 3 min. Almost pure 4-nitroazobenzene-2′-sulphenyl bromide (0·65 g.) separated. Another 0·2 g. were obtained by extraction of the mother-liquor with chloroform (total yield, 86%). Crystallisation from acetic acid gave yellow needles, m. p. 279—280°.

2-Nitroazobenzene-2′-sulphenyl Chloride.—Concentrated hydrochloric acid (60 c.c.) was added to a solution of 2-nitroazobenzene-2′-sulphenyl bromide (0·6 g.) in boiling water (500 c.c.). On saturation with salt and cooling in ice, the *chloride* separated (0·45 g., 86%). Crystallisation from toluene gave yellow needles, m. p. 237—239° (Found : C, 49·5; H, 2·7; N, 14·1. $C_{12}H_8O_2N_3SCl$ requires C, 49·1; H, 2·7; N, 14·3%).

The *4-nitro-isomer* crystallised from acetic acid as yellow plates, m. p. 258—259° (Found : C, 49·4; H, 2·8%).

4-Nitroazobenzene-2′-sulphenyl Iodide.—A solution of potassium iodide (1·5 g.) in water (10 c.c.) was added to 4-nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in boiling water (200 c.c.). On cooling, *4-nitroazobenzene-2′-sulphenyl iodide* (0·35 g., 62%) separated. Crystallisation from ethanol gave violet-brown needles, m. p. 200—202° (Found : C, 37·3; H, 2·1. $C_{12}H_8O_2N_3SI$ requires C, 37·4; H, 2·1%).

The *2-nitro-isomer*, formed in 87% yield as an immediate precipitate, m. p. 149—150° (Found : C, 37·9; H, 2·2; N, 10·7. $C_{12}H_8O_2N_3SI$ requires C, 37·4; H, 2·1; N, 10·9%), could not be crystallised from ethanol or benzene, since it readily dissociated into iodine and pure di-[*o*-(*o*-nitrophenylazo)phenyl] disulphide.

2-Nitroazobenzene-2′-sulphenyl Perchlorate.—A solution of sodium perchlorate (3 g.) in water (100 c.c.) was added to a solution of 2-nitroazobenzene-2′-sulphenyl bromide (0·7 g.) in water (500 c.c.) at 60°. On cooling, the *perchlorate* separated (0·5 g., 67%). Crystallisation from ethanol gave yellow needles, m. p. 176° (with detonation) (Found : C, 40·3; H, 2·4. $C_{12}H_8O_6N_3SCl$ requires C, 40·3; H, 2·4%).

The *4-nitro*-salt formed yellow-brown needles, m. p. 204° (with detonation), from ethanol (Found : C, 40·6; H, 2·5%).

2-Nitroazobenzene-2′-sulphenyl Cyanide (*2-Nitro-2′-thiocyanatoazobenzene*).—A solution of potassium cyanide (1 g.) in water (20 c.c.) was added to a solution of 2-nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in hot water (600 c.c.). The precipitate of *cyanide* was collected (0·4 g., 95%). Crystallisation from benzene gave yellow needles, m. p. 144° (Found : C, 55·3; H, 2·7; N, 20·1. $C_{13}H_8O_2N_4S$ requires C, 54·9; H, 2·8; N, 19·7%).

The *4-nitro-cyanide* crystallised from benzene as orange needles, m. p. 160° (Found : C, 55·3; H, 2·7; N, 19·9%).

2-Nitroazobenzene-2′-sulphenyl Thiocyanate.—A solution of 2-nitroazobenzene-2′-sulphenyl bromide (0·5 g.) in water (600 c.c.) was treated with potassium thiocyanate. The precipitated *thiocyanate* (0·4 g., 86%) crystallised from benzene as yellow-orange needles, m. p. 132° (Found : C, 50·0; H, 2·3; N, 17·8. $C_{13}H_8O_2N_4S_2$ requires C, 49·4; H, 2·5; N, 17·7%).

The *4-nitro-thiocyanate* (86%), formed at 60°, crystallised from benzene as reddish-brown needles or plates (after drying in a vacuum) which decompose at 200° (Found : C, 49·2; H, 2·6; N, 18·2%). In air, 1 mol. of water was quickly absorbed and the colour changed to orange-yellow (Found : C, 47·2; H, 3·1; N, 16·7. $C_{13}H_8O_2N_4S_2,H_2O$ requires C, 46·7; H, 3·0; N, 16·7%).

4-Nitroazobenzene-2′-sulphenyl Tribromide.—2-Benzylthio-4′-nitroazobenzene (2 g.), bromine (2 g., 2·1 mols.), and acetic acid (80 c.c.) were refluxed for 3 min. On cooling, almost pure *4-nitroazobenzene-2′-sulphenyl tribromide* separated (2·5 g., 89%). Crystallisation from acetic acid containing a small amount of bromine gave a yellow powder, m. p. 232° (decomp.) (Found : C, 29·1; H, 1·6; Br, 48·4. $C_{12}H_8O_2N_3SBr_3$ requires C, 28·9; H, 1·6; Br, 48·2%).

Action of Sodium Hydroxide on 4-Nitroazobenzene-2′-sulphenyl Tribromide.—The tribromide (1 g.) was dissolved in water (40 c.c.) containing sodium hydroxide (0·5 g.). No intermediate blue colour developed. On addition of salt, sodium 4-nitroazobenzene-2-sulphinate separated (0·5 g., 80%). Acidification of its aqueous solution with hydrochloric acid precipitated almost quantitatively 4-nitroazobenzene-2′-sulphinic acid; it crystallised from methanol as brown-yellow needles, m. p. and mixed m. p. 133—134°.

Action of Sodium Hydroxide on 2-Nitroazobenzene-2′-sulphenyl Tribromide.—2-Benzylthio-2′-nitroazobenzene (1 g.), bromine (1 g.), and acetic acid (50 c.c.) were refluxed for 3 min. After

cooling, the dark, fuming precipitate of 2-nitroazobenzene-2′-sulphenyl tribromide was collected (1 g.). It quickly lost bromine, being converted into 2-nitroazobenzene-2′-sulphenyl bromide. The freshly filtered crude tribromide (1 g.) was quickly treated with aqueous sodium hydroxide (0·5 g. in 30 c.c.). No blue colour developed. The red solution was filtered and sodium 2-nitroazobenzene-2′-sulphinate was salted out (0·5 g., 80%). Acidification of its aqueous solution with hydrochloric acid yielded almost quantitatively the free sulphinic acid, which crystallised from aqueous methanol as light yellow prisms, m. p. and mixed m. p. 144—145°.

Action of Sodium Sulphide on Di-[o-(o-*nitrophenylazo*)*phenyl*] *Disulphide.*—To a suspension of the disulphide (0·4 g.) in ethanol (50 c.c.) a solution of sodium sulphide nonahydrate (0·4 g.) in 5% aqueous sodium hydroxide (10 c.c.) was added, and the mixture refluxed for 5 min. The clear red solution was cooled, diluted with water, and acidified. A yellow precipitate consisting mainly of 2-mercapto-2′-nitroazobenzene was filtered off (0·25 g., 63%; m. p. 98—100°). On storage or on attempted crystallisation it became insoluble in ethanolic sodium hydroxide.

A solution of the freshly prepared crude thiol (0·15 g.) in 10% aqueous sodium hydroxide (3 c.c.) and ethanol (10 c.c.) was refluxed for 5 min. with benzyl chloride (0·2 c.c.). On concentration of the solution and cooling, 2-benzylthio-2′-nitroazobenzene crystallised (~0·1 g., 57%). Crystallisation from light petroleum gave orange needles, m. p. and mixed m. p. 115—116°.

The experiment was repeated, but benzyl chloride was replaced by methyl sulphate (0·2 c.c.). 2-*Methylthio-2′-nitroazobenzene* was obtained (~0·1 g., 64%). Crystallisation from ethanol gave orange needles, m. p. 114—115° (Found: C, 57·2; H, 3·8; N, 15·2. $C_{13}H_{11}O_2N_3S$ requires C, 57·2; H, 4·0; N, 15·4%). The same product (0·2 g., 61%) was obtained on shaking the red solution, obtained on reduction of the disulphide (0·3 g.) with sodium sulphide, with 1% aqueous sodium hydroxide (100 c.c.) and methyl sulphate (2 c.c.).

Action of Sodium Sulphide on Di-[o-(p-*nitrophenylazo*)*phenyl*] *Disulphide.*—A solution of sodium sulphide nonahydrate (0·5 g.) in water (10 c.c.) and 10% aqueous sodium hydroxide (5 c.c.) was added to a suspension of the disulphide in boiling ethanol (30 c.c.), and the mixture was refluxed for 10 min. The resultant red solution was filtered hot and 70% perchloric acid (2 c.c.) was added. On addition of water and cooling, the violet *di-*[o-(p-*aminophenylazo*)-*phenyl*] *disulphide diperchlorate* separated (0·35 g., 55%). Crystallisation from aqueous ethanol gave violet needles, m. p. 240° (with detonation) (Found: C, 44·3; H, 3·2; N, 13·0. $C_{24}H_{20}N_6S_2,2HClO_4$ requires C, 43·9; H, 3·3; N, 12·8%).

To a solution of the pure perchlorate (0·2 g.) in 50% aqueous ethanol (30 c.c.) 10% aqueous sodium hydrogen carbonate (10 c.c.) was added. The solution was extracted with benzene, from which light petroleum precipitated *di-*[o-(p-*aminophenylazo*)*phenyl*] *disulphide* (0·1 g., 72%). Crystallisation from benzene–light petroleum gave a yellow-brown powder, m. p. 124° (Found: C, 63·4; H, 4·4. $C_{24}H_{20}N_6S_2$ requires C, 63·1; H, 4·4%).

Pure perchlorate (0·2 g.), ethanol (30 c.c.), 10% aqueous sodium hydroxide (10 c.c.), and benzoyl chloride (2 c.c.) were shaken for 30 min. On addition of water, *di-*[o-(p-*benzamido*-*phenylazo*)*phenyl*] *disulphide* separated (0·15 g., 74%). Crystallisation from ethanol gave a yellow powder, m. p. 190—192° (Found: C, 68·8; H, 3·9; N, 13·1. $C_{38}H_{28}N_6O_2S_2$ requires C, 68·7; H, 4·2; N, 12·7%).

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19. *o-Mercapto-azo-compounds. Part IX.* Debenzylation of 1-Benzylthio-2-phenylazonaphthalene.*

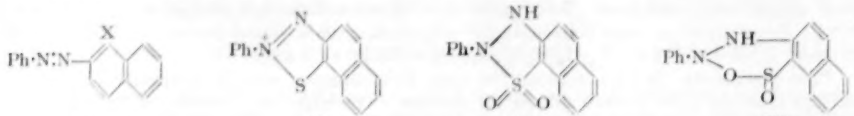
By A. Burawoy, A. Chaudhuri, and W. I. Hyslop.

The debenzylation of 1-benzylthio-2-phenylazonaphthalene by bromine in glacial acetic acid and the action of sodium in liquid ammonia on 2-benzylthioazobenzene, 1-benzylthio-2-phenylazonaphthalene, and 2 : 2′-dibenzylthioazobenzene are investigated. The preparation and the properties of 2-phenylazonaphthalene-1-sulphenyl bromide and its derivatives, of 2-phenylazonaphthalene-1-sulphinic acid, and of 1-mercapto-2-phenylazonaphthalene are discussed.

The investigation of the debenzylation of 2-benzylthioazobenzene and its derivatives (Parts V—VIII *) has been extended to 1-benzylthio-2-phenylazonaphthalene (I; X = S·CH_2Ph) which is obtained by condensing 1-benzylthio-2-naphthylamine with nitrosobenzene in acetic acid. Heating with 1 and 2 mols. of bromine in acetic acid yields almost quantitatively 2-phenylazonaphthalene-1-sulphenyl bromide and tribromide respectively (I; X = SBr and SBr_3).

The sulphenyl bromide is stable to heat, soluble in water, and converted in aqueous solution by double decomposition into the chloride, iodide, thiocyanate, perchlorate, and water-insoluble cyanide. The iodide is sufficiently stable to allow crystallisation from ethanol and shows characteristic colour changes in solvents similar to those already observed for azobenzene-2-sulphenyl iodide (see Part VI). The chloride crystallises with 1 mol. of water which cannot be removed without decomposition which starts slowly above 100°; but its identity is not in doubt, since it is easily soluble in water and converted quantitatively by potassium cyanide in aqueous solution into the almost pure cyanide (1-thiocyanato-2-phenylazonaphthalene).

The properties of these compounds are very similar to those of the corresponding azobenzene-2-sulphenyl derivatives (see Part VI). Like the latter, except for the cyanide, they will exist in the solid state and in solution completely or partly as true salts of structure (II), involving a 2-phenylnaphtho(2′ : 1′-4 : 5)-1-thia-2 : 3-diazolium cation.



(I) (II) (III) (IV)

2-Phenylazonaphthalene-1-sulphenyl tribromide (in dilute ethanol) is converted almost quantitatively by sodium hydroxide into the orange sodium 2-phenylazonaphthalene-1-sulphinate (I; X = SO_2Na), but the free acid obtained by acidification crystallises from benzene and light petroleum as colourless plates, indicating the absence of an azo-group. Being similar to the almost colourless azobenzene-2-sulphinic acid (see Part V), it should possess the cyclic structure (III) or (IV). However, whereas the azobenzene derivative is fairly stable and can be crystallised from dilute ethanol, 2-phenylazonaphthalene-1-sulphinic acid in chloroform, ether, or ethanol dissociates, slowly at room temperature, quickly on heating, into 2-phenylazonaphthalene (I; X = H) and sulphur dioxide and, thus, cannot be crystallised from these solvents.

The sulphinic acid also dissociates when melted or when its alkaline solution is heated. Attempts to prepare the 4-nitrobenzyl and methyl sulphones by treating the aqueous solutions of the sodium sulphinate at room temperature with 4-nitrobenzyl chloride and methyl sulphate respectively also failed, 2-phenylazonaphthalene being the only product isolated. The stability of the sulphinic acid in non-polar solvents such as benzene and light petroleum, and the qualitative observation that the rate of dissociation increases in

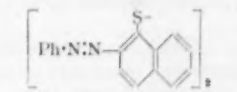
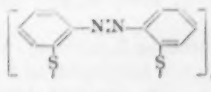
* Parts V—VIII, *J.*, 1954, 90, 4481; 1955, 3798; preceding paper.

the order of solvents chloroform < ether < ethanol, suggest that the decomposition is initiated by ionisation and subsequent tautomerisation to the true, but unstable, 2-phenylazonaphthalene-1-sulphinic acid (I; X = SO_2H). This is similar to the slow conversion of the colourless "azobenzene-2-sulphinic acid" in chloroform or ethanol into the orange-yellow, but in this case stable, true azo-tautomer. Kharasch, King, and Bruice (*J. Amer. Chem. Soc.*, 1955, **77**, 981) recently reported that 2 : 4-dinitrobenzenesulphenyl chloride on treatment with alkali or acid yields, in place of the expected sulphinic acid, only *m*-dinitrobenzene. The instability of both these sulphinic acids should be due to the strain resulting from intramolecular steric hindrance between the SO_2H group and the large *ortho*-substituents.

The structures of the sulphenyl derivatives and of the colourless tautomers of the sulphinic acids, and the quantitative aspects of their solvent-dependent equilibria and gradual tautomeric changes, are being further investigated.

On addition of an excess of sodium hydroxide, azobenzene-2-sulphenyl bromide and its derivatives in dilute ethanol are converted into the corresponding blue sodium sulphenates which at room temperature only slowly disproportionate to the insoluble disulphides and soluble sodium sulphinates. In contrast, 2-phenylazonaphthalene-1-sulphenyl bromide, when similarly treated, immediately yields a precipitate of di-(2-phenylazo-1-naphthyl) disulphide (V), also obtained by the action of zinc, and the soluble sodium 2-phenylazonaphthalene-1-sulphinate (I; X = SO_2Na), the intermediate formation of a blue sodium sulphenate (I; X = SONa) not being observed. Unexpectedly, a very small amount of 2-phenylazo-1-naphthol was also isolated.

The debenzylation of the *o*-benzylthioazo-compounds with sodium in liquid ammonia, a method originally applied by Sifferd and du Vigneaud (*J. Biol. Chem.*, 1935, **108**, 757) to the cleavage of benzylcysteine, has also been investigated. Whereas 2-benzylthioazobenzene itself, probably owing to its insolubility, remains unchanged even in presence of ether, 1-benzylthio-2-phenylazonaphthalene is easily debenzylated, the disulphide (V) or, in presence of an excess of sodium, the sodium salt (I; X = SNa) of 1-mercapto-2-phenylazonaphthalene being formed. The latter is also obtained by reduction of the disulphide with ethanolic sodium sulphide.

(V)   (VI)

Like 2-mercaptoazobenzene, the crude thiol formed on acidification could not be purified, being readily reoxidised on storage or attempted crystallisation to the disulphide, but its identity has been established by conversion into the original 1-benzylthio-2-phenylazonaphthalene.

Similarly, 2 : 2′-dibenzylthioazobenzene yields, depending on the quantity of sodium used, the polysulphide (VI) or the sodium salt of 2 : 2′-dimercaptoazobenzene, the preparations of which, by the action of zinc or sodium hydroxide on di-[*o*-(*o*-bromothio)-phenylazophenyl] disulphide and by the reduction of the polysulphide with sodium sulphide respectively, have already been described (see Part VII).

Experimental

1-Benzylthio-2-phenylazonaphthalene.—A solution of 1-benzylthio-2-naphthylamine (8 g.) and nitrosobenzene (4·0 g.) in acetic acid (60 c.c.) was kept for 24 hr. at room temperature. The precipitate of *1-benzylthio-2-phenylazonaphthalene* was filtered off and washed with a little acetic acid and light petroleum (7·5 g., 70%). Crystallisation from ethanol gave orange-red needles, m. p. 122° (Found: C, 78·2; H, 5·2; N, 7·9. $C_{23}H_{18}N_2S$ requires C, 78·0; H, 5·1; N, 7·9%).

2-Phenylazonaphthalene-1-sulphenyl Bromide.—A solution of 1-benzylthio-compound (5 g.) and bromine (2·26 g., 1 mol.) in glacial acetic acid (80 c.c.) was refluxed for 3 min. On cooling, almost pure *sulphenyl bromide* separated (4 g., 82%). Less pure product (0·3 g.) was obtained by extracting the filtrate with chloroform. Crystallisation from acetic acid gave long yellow needles, m. p. 245°. The bromide is soluble in water, alcohol, chloroform, and sparingly so in benzene (Found: C, 56·2; H, 2·9; N, 8·3. $C_{16}H_{11}N_2SBr$ requires C, 56·0; H, 3·2; N, 8·2%).

2-*Phenylazonaphthalene*-1-*sulphenyl Chloride*.—A solution of the bromide (0·5 g.) in water (200 c.c.) and concentrated hydrochloric acid (50 c.c.) was extracted with chloroform. The extract was concentrated, and the *sulphenyl chloride* (0·3 g., 69%) precipitated by addition of light petroleum. Crystallisation from chlorobenzene gave hydrated yellow needles, m. p. 222°, easily soluble in water (Found : C, 60·7; H, 4·0; Cl, 11·5. $C_{16}H_{11}N_2SCl,H_2O$ requires C, 60·6; H, 4·1; Cl, 11·2%). No loss of weight was observed at 100° in 6 hr. and slow decomposition above this temperature.

2-*Phenylazonaphthalene*-1-*sulphenyl Iodide*.—Potassium iodide (1 g.) in water (20 c.c.) was added to a solution of the sulphenyl bromide (0·5 g.) in water (200 c.c.). The precipitate of the *iodide* (formed almost quantitatively) crystallised from ethanol as almost black needles, m. p. 228°, sparingly soluble in solvents with the following colours : water, yellow; ethanol, orange; chloroform, deep green; benzene, green (Found : C, 48·4; H, 2·8. $C_{16}H_{11}N_2SI$ requires C, 49·0; H, 2·8%).

2-*Phenylazonaphthalene*-1-*sulphenyl Perchlorate*.—Sodium perchlorate (1 g.) in water (10 c.c.) was added to a solution of the sulphenyl bromide (0·3 g.) in water (100 c.c.). The precipitated *perchlorate* (formed almost quantitatively) was crystallised from ethanol as yellow needles, m. p. 216° (decomp.) (Found : C, 52·6; H, 3·0; N, 8·0. $C_{16}H_{11}O_4N_2SCl$ requires C, 52·9; H, 3·0; N, 7·7%).

2-*Phenylazonaphthalene*-1-*sulphenyl Thiocyanate*.—Potassium thiocyanate (1 g.) in water (20 c.c.) was added to a solution of the sulphenyl bromide (0·5 g.) in water (200 c.c.). The precipitated *thiocyanate* (0·35 g., 74%) crystallised from ethanol as orange needles, m. p. 160° (Found : C, 63·6; H, 3·4; N, 13·0. $C_{17}H_{11}N_3S_2$ requires C, 63·5; H, 3·4; N, 13·0%).

2-*Phenylazonaphthalene*-1-*sulphenyl Cyanide* (1-*Thiocyanato*-2-*phenylazonaphthalene*).—The above experiment was repeated, but potassium thiocyanate was replaced by potassium cyanide. The insoluble 1-*thiocyanato*-2-*phenylazonaphthalene* was collected (0·4 g., 95%). Crystallisation from ethanol gave orange needles, m. p. 116° (Found : C, 70·8; H, 3·9; N, 14·1. $C_{17}H_{11}N_3S$ requires C, 70·6; H, 3·8; N, 14·5%). 2-Phenylazonaphthalene-1-sulphenyl chloride hydrate was similarly and quantitatively converted into the cyanide.

2-*Phenylazonaphthalene*-1-*sulphenyl Tribromide*.—A solution of 1-benzylthio-2-phenylazonaphthalene (2 g.) and bromine (1·9 g., 2·1 mols.) in acetic acid (45 c.c.) was refluxed for 3 min. On cooling, pure 2-*phenylazonaphthalene*-1-*sulphenyl tribromide* separated (2·2 g., 76%). Crystallisation from acetic acid containing a drop of bromine gave yellow-brown plates, m. p. 170—171° (Found : C, 38·4; H, 2·3; Br, 47·1. $C_{16}H_{11}N_2SBr_3$ requires C, 38·2; H, 2·2; Br, 47·6%).

2-*Phenylazonaphthalene*-1-*sulphinic Acid*.—An excess of 10% aqueous sodium hydroxide (10 c.c.) was added to a suspension of 2-phenylazonaphthalene-1-sulphenyl tribromide (0·5 g.) in ethanol (50 c.c.). The resultant deep red solution was diluted with water (200 c.c.) and acidified with hydrochloric acid. The precipitated 2-*phenylazonaphthalene*-1-*sulphinic acid* was washed with light petroleum (0·2 g., 66%). Crystallisation from benzene–light petroleum (b. p. 60—80°) gave colourless plates, m. p. 146—148° (Found : C, 65·0; H, 4·1; N, 9·3; active H, 0·32. $C_{16}H_{11}N_2{\cdot}SO_2H$ requires C, 64·9; H, 4·1; N, 9·4; active H, 0·34%). The sulphinic acid, when heated at its m. p. for a few minutes, dissociated quantitatively into 2-phenylazonaphthalene and sulphur dioxide. Crystallisation from ethanol gave orange-yellow needles, m. p. 84° [Bucherer and Rauch (*J. prakt. Chem.*, 1931, **132**, 259) give m. p. 84°] (Found : C, 82·4; H, 5·1; N, 12·4. Calc. for $C_{16}H_{12}N_2$: C, 82·7; H, 5·1; N, 12·1%).

Di-(2-*phenylazo*-1-*naphthyl*) *Disulphide*.—A solution of 2-phenylazonaphthalene-1-sulphenyl bromide (1 g.) in water (400 c.c.) and benzene (50 c.c.) was stirred for 3 hr. with zinc dust (7 g.). After filtration, the benzene layer was dried and concentrated to a small volume. The *disulphide* was collected (0·6 g., 80%) and crystallised from benzene as red prisms, m. p. 205° (Found : C, 73·1; H, 4·2; N, 10·5. $C_{32}H_{22}N_4S_2$ requires C, 73·0; H, 4·2; N, 10·6%). Treatment of the tribromide with zinc gave the same disulphide.

1-*Mercapto*-2-*phenylazonaphthalene*.—A solution of sodium sulphide nonahydrate (1 g.) in water (10 c.c.) was added to a suspension of finely ground disulphide (0·5 g.) in ethanol (50 c.c.). After 24 hours' stirring, water (150 c.c.) was added and the filtered red solution acidified with hydrochloric acid. The precipitated crude 1-mercapto-2-phenylazonaphthalene was dried (0·33 g., 70%). It slowly lost its solubility in ethanolic sodium hydroxide. Crystallisation from light petroleum (b. p. 40—60°) or from benzene yielded the pure disulphide, m. p. 205°.

The experiment was repeated, but 10% aqueous sodium hydroxide (10 c.c.) and benzyl chloride (2 c.c.) were added with stirring to the filtered red solution. After 15 min., the precipitate of 1-benzylthio-2-phenylazonaphthalene was collected [0·6 g., 89%; m. p. and

mixed m. p. 122° (from ethanol)]. The same product (0·08 g., 75%) was obtained on stirring a filtered solution of freshly prepared crude 1-mercapto-2-phenylazonaphthalene (0·08 g.) in cold ethanol (50 c.c.) and 10% aqueous sodium hydroxide (5 c.c.) with a drop of benzyl chloride and subsequent addition of water.

Action of Sodium Hydroxide on 2-Phenylazonaphthalene-1-sulphenyl Bromide.—10% Aqueous sodium hydroxide (20 c.c.) was added to 2-phenylazonaphthalene-1-sulphenyl bromide (2 g.) in cold ethanol (50 c.c.). The precipitate of disulphide formed immediately was collected (0·8 g., 78%). Crystallisation from benzene gave red prisms, m. p. 205°, identical with the disulphide obtained by the action of zinc.

The alkaline filtrate was acidified and the pink precipitate, consisting mainly of 2-phenylazonaphthalene-1-sulphinic acid, was filtered off and washed with light petroleum (0·35 g., 41%). Crystallisation from benzene and light petroleum (b. p. 60—80°) gave colourless plates, m. p. 146—148°, identical with the sulphinic acid obtained by the action of sodium hydroxide on the tribromide. The mother-liquors contained a small amount of 2-phenylazo-1-naphthol which crystallised from ethanol as red needles, m. p. and mixed m. p. 138°.

Action of Sodium in Liquid Ammonia on 2-Benzylthioazobenzene.—2-Benzylthioazobenzene (0·5 g.) or its solution in ether was added to a solution of sodium (0·3 g., 6 atomic proportions) in liquid ammonia (50 c.c.) below −50°. (The ammonia was previously treated with a small amount of sodium until a permanent blue colour was attained.) After 8 hours' stirring, addition of ammonium chloride (0·3 g.), and evaporation of ammonia, unchanged starting material was recovered quantitatively.

Action of Sodium in Liquid Ammonia on 1-Benzylthio-2-phenylazonaphthalene.—1-Benzylthio-2-phenylazonaphthalene (0·5 g.) was added to a solution of sodium (0·1 g., 3 atomic proportions) in liquid ammonia (50 c.c.) below −50°. After 5 hours' stirring ammonium chloride (0·2 g.) was added and ammonia evaporated. The residue of almost pure di-(2-phenylazo-1-naphthyl) disulphide was washed with water and filtered off [0·32 g., 86%; m. p. 198—200° (crude), 205° (from benzene)].

The experiment was repeated with 0·2 g. of sodium and without ammonium chloride. The residue was extracted with cold water and the insoluble disulphide collected [0·11 g., 29%; m. p. 195° (crude)]. The aqueous extract, after addition of 5% aqueous sodium hydroxide (5 c.c.) and ethanol (10 c.c.), was quickly shaken with benzyl chloride (2 c.c.), and the precipitate of 1-benzylthio-2-phenylazonaphthalene collected [0·24 g., 48%; m. p. and mixed m. p. 122° (from ethanol)].

The experiment was repeated, but the aqueous extract quickly acidified. The precipitated 1-mercapto-2-phenylazonaphthalene was filtered off and redissolved in ethanolic sodium hydroxide, and the filtered solution was shaken with benzyl chloride. 1-Benzylthio-2-phenylazonaphthalene was collected [0·22 g., 44%; m. p. 122° (from ethanol)].

Action of Sodium in Liquid Ammonia on 2 : 2′-Dibenzylthioazobenzene.—2 : 2′-Dibenzylthioazobenzene (0·5 g.) was added to a solution of sodium (0·11 g., 4 atomic proportions) in liquid ammonia (50 c.c.) below −50°. After 3 hours' stirring, ammonium chloride (0·1 g.) was added and ammonia allowed to evaporate. The residue of the polysulphide (VI) was washed with water and benzene [0·25 g., 87%; m. p. 266—268° (before and after crystallisation from chlorobenzene–nitrobenzene), not depressed by an authentic specimen (see Part VII)].

The experiment was repeated with 0·2 g. of sodium and without ammonium chloride. The residue, consisting of the sodium salt of 2 : 2′-dimercaptoazobenzene, was dissolved in water, and the solution was filtered and shaken with benzyl chloride (2 c.c.). The precipitate of 2 : 2′-dibenzylthioazobenzene was collected [0·37 g., 74%; m. p. and mixed m. p. 222° (from toluene)].

The last experiment was repeated, but the filtered aqueous solution was acidified. The precipitate of crude 2 : 2′-dimercaptoazobenzene was filtered off, dried in a vacuum desiccator for 20 hr. (0·17 g., 54%), and dissolved in aqueous sodium hydroxide (0·5 g. in 100 c.c.). When the filtered solution was shaken with methyl sulphate, 2 : 2′-dimethylthioazobenzene separated [0·12 g., 38%; m. p. 155° (from ethanol), not depressed by an authentic specimen (see Part VII)].

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20. *The Chemotherapy of Tuberculosis. Part VII.* Thiosemicarbazones of Substituted Phenyl- and Pyridyl-benzaldehydes.*

By J. Cymerman-Craig and J. W. Loder.

The preparation of 4′-ethoxycarbonyl-, 4′-carboxy-, and 4′-methoxydiphenyl-4-aldehyde is described. The isosteric *p*-2-pyridylbenzaldehyde has been obtained by two synthetical routes, and the thiosemicarbazones of these aldehydes and of some related compounds have been tested against *Mycobacterium tuberculosis*.

The discovery of the tuberculostatic activity of *p*-substituted benzaldehyde thiosemicarbazones (Behnisch, Mietzsch, and Schmidt, *Angew. Chem.*, 1948, **60**, 113) prompted us to examine some derivatives of diphenyl-4-aldehydes. Diphenyl-4-aldehyde thiosemicarbazone proved highly active *in vitro*, and in view of its low solublity more soluble analogues were investigated. The only recorded example of the Gomberg and related reactions in which the product is an aldehyde is the action of *N*-nitrosoacetanilide on benzaldehyde (Grieve and Hey, *J.*, 1934, 1798) which afforded a mixture of isomers, including diphenyl-4-aldehyde. The unknown *p*-ethoxycarbonyl-*N*-nitrosoacetanilide could not be prepared by the action of nitrous fumes on the acetanilide which is thus similar to *p*-nitroacetanilide; the latter forms the nitroso-derivative with nitrosyl chloride (Haworth and Hey, *J.*, 1940, 361).

p-Ethoxycarbonylbenzenediazonium chloride coupled with benzaldehyde in the presence of sodium acetate to give, in low yield, 4′-ethoxycarbonyldiphenyl-4-aldehyde; acid hydrolysis of the ester group then gave 4′-carboxydiphenyl-4-aldehyde. A dicarboxylic acid, obtained as a by-product, had the properties expected for diphenyl-4 : 4′-dicarboxylic acid, and the same substance was obtained by acid hydrolysis of 4′-ethoxycarbonyldiphenyl-4-aldehyde thiosemicarbazone and oxidation of the product. Work directed towards a rigid proof of structure of 4′-carboxydiphenyl-4-aldehyde is in progress.

Condensation of *p*-methoxybenzenediazonium chloride and benzaldehyde gave only a minute yield of impure 4′-methoxydiphenyl-4-aldehyde, while the use of *p*-methoxy-*N*-nitrosoacetanilide afforded the crude aldehyde in 14·5% yield. The zinc cyanide modification (Adams and Montgomery, *J. Amer. Chem. Soc.*, 1924, **46**, 1518) of the Gattermann aldehyde synthesis failed with 4-hydroxydiphenyl. Attempted formylation of 4-methoxydiphenyl with *N*-methylformanilide and phosphorus oxychloride was unsuccessful, nor could a chloromethyl derivative be obtained from this compound by using chloromethyl ether and zinc chloride. An attempted reduction of 4′-methoxydiphenyl-4-carbonyl chloride with lithium hydride by Brandt's method (*Acta Chem. Scand.*, 1949, **3**, 1050) gave no aldehydic material.

4-Cyano-4′-hydroxydiphenyl was synthesised from 4′-amino-4-cyanodiphenyl with a view to using Stephen's aldehyde synthesis (*J.*, 1925, 1874); this route was not pursued, however, as the desired aldehyde was obtained by McFadyen and Stevens's method (*J.*, 1936, 584). Derivatives of the product were identical with those of the aldehyde previously obtained from *p*-methoxy-*N*-nitrosoacetanilide and benzaldehyde, thus confirming the 4 : 4′-orientation of the substituents.

The isosteric *p*-pyridylbenzaldehyde derivative was prepared in order to overcome the low water-solubility of the tuberculostatically active diphenyl-4-aldehyde. Diazotisation of *p*-2-pyridylaniline by the method of Butterworth, Heilbron, and Hey (*J.*, 1940, 355) followed by treatment with cuprous cyanide and hydrolysis gave a mixture of *p*-chloro-2-pyridylbenzene and *p*-2-pyridylbenzoic acid. Under the strongly acidic conditions used, partial conversion of some cuprous cyanide into the chloride may have occurred, the chloride then reacting by a normal Sandmeyer reaction.

In view of the poor yield obtained in this synthesis, an alternative route was devised making use of the known addition of organolithium compounds exclusively to the carbon

* Part VI, *J.*, 1955, 4315.

atom of the azomethine linkage in aromatic heterocyclic compounds (*e.g.*, Gilman and Blume, *J. Amer. Chem. Soc.*, **1943**, **65**, 2476). Reaction of *p*-tolyl-lithium with pyridine by an adaptation of Evans and Allen's method (*Org. Synth.*, Coll. Vol. II, **1944**, 517) afforded *p*-2-pyridyltoluene. While potassium permanganate failed to oxidise this compound in acetone, reaction occurred readily in hydrochloric acid, affording *p*-2-pyridylbenzoic acid. Its methyl ester, identical with that obtained from *p*-2-pyridylaniline, was readily converted, *via* the hydrazide, into the benzenesulphonylhydrazine. Decomposition of this with alkali in presence of thiosemicarbazide by Fox's method (*J. Org. Chem.*, **1952**, **17**, 555) gave the derivative directly in 25% yield.

An improved preparation of this aldehyde was the direct oxidation of *p*-2-pyridyltoluene with chromic acid in presence of acetic anhydride, which afforded *p*-2-pyridylbenzaldehyde and its diacetate, both readily giving derivatives identical with one another and with those prepared from the same aldehyde obtained by McFadyen and Stevens's method.

The thiosemicarbazones were kindly examined for antituberculous activity by Professor S. D. Rubbo; they inhibited completely the growth of *Mycobacterium tuberculosis* H37Rv *in vitro* after 14 days at 37° in Youmans's medium at dilutions of M/128,000 to M/512,000 in presence of 10% of serum. 4'-Carboxydiphenyl-4-aldehyde thiosemicarbazone was an exception in that it had greatly reduced activity (M/32,000). A full account of the bacteriological aspects will be given elsewhere.

Experimental

Diphenyl-4-aldehyde Thiosemicarbazone.—(With J. N. Baxter.) The *thiosemicarbazone*, obtained in quantitative yield, crystallised from methanol as yellowish plates, m. p. 202—202·5° (Found: C, 66·0; H, 5·2; N, 16·6; S, 12·45. $C_{14}H_{13}N_3S$ requires C, 65·85; H, 5·15; N, 16·45; S, 12·55%).

A suspension of the thiosemicarbazone (1·28 g.) in ethanol (100 c.c.) was refluxed with methyl iodide (0·6 c.c.) for 3½ hr., the resulting solution evaporated to dryness *in vacuo*, and the residue triturated with dry ether giving *diphenyl-4-aldehyde S-methylthiosemicarbazone hydriodide* (1·87 g., 92%), needles (from *iso*propanol–ether), m. p. 175—176°, after softening at 167° (Found: N, 10·75. $C_{15}H_{16}N_3SI$ requires N, 10·6%).

4'-Ethoxycarbonyldiphenyl-4-aldehyde.—A suspension of ethyl *p*-aminobenzoate (100 g.) in hydrochloric acid (330 c.c.; 10N) and water (180 c.c.) was diazotised at 0—5°, and the solution stirred vigorously with benzaldehyde (500 c.c.) at 5—10° under nitrogen while a saturated solution of sodium acetate trihydrate (330 g.) was added dropwise. After 3 days, benzaldehyde was removed by steam distillation, and was shown to be free from higher-boiling material. The residual oil was purified by dissolution in ether and the aldehyde obtained from it by formation of the bisulphite compound (18·4 g., 8%). The *thiosemicarbazone* crystallised from aqueous acetone as needles, m. p. 235° (decomp.) (Found: C, 62·4; H, 5·3; N, 13·0. $C_{17}H_{17}O_2N_3S$ requires C, 62·4; H, 5·25; N, 12·85%), and the *2:4-dinitrophenylhydrazone* formed red needles, m. p. 263°, from ethyl acetate–xylene (Found: C, 61·1; H, 4·5; N, 13·1. $C_{22}H_{18}O_6N_4$ requires C, 60·85; H, 4·2; N, 12·9%). Acid hydrolysis of the thiosemicarbazone followed by treatment of the neutralised solution with a few drops of hydrogen peroxide (10%) gave on acidification an acid (decomp. above 345°) showing the properties of diphenyl-4:4'-dicarboxylic acid.

4'-Carboxydiphenyl-4-aldehyde.—The bisulphite compound of 4'-ethoxycarbonyldiphenyl-4-aldehyde was refluxed under nitrogen with aqueous alcohol (25% v/v) containing sulphuric acid (20% v/v). The mixture was made alkaline with sodium carbonate solution and extracted with benzene. A small amount of insoluble sodium salt was obtained and afforded an acid with properties in agreement with those recorded for diphenyl-4:4'-dicarboxylic acid (Doebner, *Ber.*, 1876, **9**, 272). Acidification of the alkaline solution gave the crude carboxyaldehyde, whose *thiosemicarbazone* formed pale brown microcrystals (from aqueous acetone), m. p. 240° upwards (decomp.) (Found: C, 59·95; H, 4·7; N, 13·8. $C_{15}H_{13}O_2N_3S$ requires C, 60·15; H, 4·4; N, 14·0%), and *2:4-dinitrophenylhydrazone*, red needles (benzene–pyridine), m. p. 312° (decomp.) (Found: C, 59·6; H, 3·7; N, 13·65. $C_{20}H_{14}O_6N_4$ requires C, 59·15; H, 3·5; N, 13·8%).

4-Cyano-4'-hydroxydiphenyl.—4-Amino-4'-cyanodiphenyl, obtained by Angeletti and Gatti's

method (*Gazzetta*, 1928, **58**, 630), crystallised from toluene as buff microcrystals, m. p. 161—162°, softening at 155°. Angeletti and Gatti (*loc. cit.*) give m. p. 157°.

The amine (6·58 g.) was diazotised at 0°, and the solution diluted with an equal volume of water and filtered. The filtrate was added dropwise to a boiling solution of copper sulphate (80 g.) in water (80 c.c.) and the product obtained on filtering the cooled mixture was dissolved in potassium hydroxide solution and reprecipitated with hydrochloric acid to give *4-cyano-4'-hydroxydiphenyl* (4 g., 60%), prisms, m. p. 193—194° (after sublimation at 205°/0·3 mm.) (Found : C, 79·8; H, 4·8; N, 7·2. $C_{13}H_9ON$ requires C, 79·95; H, 4·65; N, 7·2%).

4-Acetyl-4'-methoxydiphenyl.—The 2 : 4-*dinitrophenylhydrazone* formed red needles (from toluene), m. p. 217° (Found : C, 62·25; H, 4·5; N, 13·75. $C_{21}H_{18}O_5N_4$ requires C, 62·05; H, 4·45; N, 13·8%). The *thiosemicarbazone* crystallised from benzene as yellow microcrystals, m. p. 210°, resolidifying and remelting at 290° (decomp.), which contained solvent of crystallisation not removed at 100° (Found : C, 67·2, 67·3; H, 5·8, 5·7. $C_{16}H_{17}ON_3S,\frac{1}{2}C_6H_6$ requires C, 67·4; H, 5·9%). Crystallisation from acetone–light petroleum (b. p. 60—90°) gave white microcrystals, m. p. 290° (decomp.) (Found : C, 64·0; H, 5·85. $C_{16}H_{17}ON_3S$ requires C, 64·2; H, 5·7%).

4-Acetyl-4'-hydroxydiphenyl.—4-Acetyl-4'-methoxydiphenyl (1·5 g.) (Johnson, Gutsche, and Offenhauer, *J. Amer. Chem. Soc.*, 1946, **68**, 1648), acetic acid (20 c.c.), and hydrobromic acid (5·2 c.c.; 48%) were refluxed for 6·5 hr. The mixture was poured into water and gave a quantitative yield of the ketone, m. p. 202°. Fieser and Bradsher (*J. Amer. Chem. Soc.*, 1936, **58**, 1738) give m. p. 205—206° for the compound prepared by the Fries reaction. The 2 : 4-*dinitrophenylhydrazone* crystallised as red needles (from aqueous acetic acid), m. p. 250° (decomp.) (Found : C, 60·1; H, 4·25. $C_{20}H_{16}O_5N_4,\frac{1}{2}H_2O$ requires C, 60·1; H, 4·25%). The *thiosemicarbazone* formed yellow microcrystals (from acetic acid), m. p. 280° (decomp.) (Found : C, 63·6; H, 5·4. $C_{15}H_{15}ON_3S$ requires C, 63·15; H, 5·3%).

4-Methoxydiphenyl-4'-carboxyl Chloride.—Treatment of 4-methoxydiphenyl-4'-carboxylic acid (Johnson, Gutsche, and Offenhauer, *loc. cit.*) with thionyl chloride gave the acid chloride, which formed yellow crystals, m. p. 97—98°, from light petroleum (b. p. 90—100°). The methyl ester had m. p. 171—172° (Fieser and Bradsher, *loc. cit.*, give m. p. 172—173°).

4-Methoxydiphenyl-4'-carboxyhydrazide.—Methyl 4-methoxydiphenyl-4'-carboxylate (13·3 g.), hydrazine hydrate (13 c.c.; 100%), and 2-ethoxyethanol (30 c.c.) were refluxed for 3·25 hr., and on cooling gave plates of the *hydrazide* (10·44 g., 79%), m. p. 203—204° (Found : C, 69·2; H, 5·75; N, 11·5. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·85; N, 11·55%).

N-(4'-Methoxydiphenyl-4-carbonyl)-N'-benzenesulphonylhydrazine.—The hydrazide (9·85 g.), suspended in pyridine (160 c.c.), was treated with benzenesulphonyl chloride (5·5 c.c.) at 0°. The solution was set aside overnight at room temperature and then poured into ice and dilute hydrochloric acid, the mixture filtered, and the residue washed (water) giving the *benzenesulphonylhydrazine* (15·3 g., 99%), needles (from aqueous acetone), m. p. 208—209° (decomp.) (Found : C, 62·95; H, 4·6. $C_{20}H_{18}O_4N_2S$ requires C, 62·8; H, 4·75%).

4-Methoxydiphenyl-4'-aldehyde.—(i) A solution of the benzenesulphonylhydrazine (6 g.) in ethylene glycol (60 c.c.) was treated at 160° with anhydrous sodium carbonate (4·5 g.), added all at once. The mixture was kept at 170° for 80 sec. and then poured into hot water (200 c.c.). The *aldehyde* crystallised from light petroleum (b. p. 90—100°) as needles (1·96 g., 59%), m. p. 101·5—102° (Found : C, 79·1; H, 5·85. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·7%). The 2 : 4-*dinitrophenylhydrazone* formed red needles (from aqueous acetone), m. p. 240—241° (Found : C, 59·85; H, 4·65. $C_{20}H_{16}O_6N_4,\frac{1}{2}H_2O$ requires C, 59·85; H, 4·3%). The *thiosemicarbazone* crystallised from aqueous alcohol as yellow microcrystals, m. p. 212—213° (decomp.) (Found : C, 62·75; H, 5·6. $C_{15}H_{15}ON_3S$ requires C, 63·1; H, 5·3%).

(ii) A solution of *p*-methoxy-*N*-nitrosoacetanilide (17·4 g.; Haworth and Hey, *J.*, 1940, 361) in benzaldehyde (200 c.c.) was dried (Na_2SO_4) and set aside at room temperature in an atmosphere of nitrogen for 24 hr., then warmed to 50° for 1 hr., and finally distilled with steam. The residue was purified *via* the bisulphite compound (4·2 g., 14·5%). It afforded a 2 : 4-dinitrophenylhydrazone, m. p. 241—242°, and a thiosemicarbazone, m. p. 213°, undepressed with the derivatives prepared in (i).

Sandmeyer Reaction with p-2-*Pyridylaniline Dihydrochloride.*—Diazotisation of *p*-2-pyridylaniline (m. p. 310—313°; Forsyth and Pyman, *J.*, 1926, 2912, record m. p. >310°) and treatment of the salt with cuprous cyanide was carried out by Butterworth, Heilbron, and Hey's method (*J.*, 1940, 355). The product (42%) was a mixture and was hydrolysed directly with sodium hydroxide solution (20%). The non-acidic portion crystallised from light petroleum (b. p. 40—60°) as flat needles, m. p. 52—53° (picrate, m. p. 169°, from methanol) and was thus

p-chloro-2-pyridylbenzene (lit., m. p. 52—53°; picrate, m. p. 169—170°). The crude acid was esterified with methanol and concentrated sulphuric acid giving methyl *p*-2-pyridylbenzoate as prisms, m. p. 97° alone and mixed with a sample from the alternative synthesis (below). Butterworth, Heilbron, and Hey (*loc. cit.*) give m. p. 90°.

p-2-*Pyridyltoluene*.—*p*-Tolyl-lithium, prepared from *p*-bromotoluene (39 g.) by Gilman, Zoellner, and Selby's method (*J. Amer. Chem. Soc.*, 1932, **54**, 1957), was treated with anhydrous pyridine by Evans and Allen's method (*Org. Synth.*, Coll. Vol. II, 1944, p. 517) except that the toluene solution was refluxed for 7 hr. Distillation gave p-2-*pyridyltoluene* as a pale yellow oil (23·6 g., 61%), b. p. 140—142°/2 mm., 91—92°/0·001 mm., n_D^{18} 1·6160 (Found: N, 8·1. $C_{12}H_{11}N$ requires N, 8·25%), which slowly darkened. The *picrate* crystallised from ethanol as yellow prisms, m. p. 180—180·5° (Found: N, 14·4. $C_{12}H_{11}N,C_6H_3O_7N_3$ requires N, 14·1%).

p-2-*Pyridylbenzoic Acid*.—A solution of *p*-2-pyridyltoluene (8·55 g.) in hydrochloric acid (8·55 c.c.; 10N) and water (150 c.c.) was treated at 100° with powdered potassium permanganate (22·6 g.) during 0·5 hr. with vigorous stirring. Heating and stirring were continued for a further 0·5 hr., and the precipitate was then extracted repeatedly with boiling sodium carbonate solution. The combined extracts were extracted with ether (the non-acidic material gave a picrate, m. p. 180·5°, corresponding to 12% of *p*-2-pyridyltoluene), and concentrated *in vacuo*. Cautious acidification gave the acid (5·67 g., 60%), m. p. 232—232·5° (Butterworth, Heilbron, and Hey, *loc. cit.*, give m. p. 232°); the methyl ester (61%) had m. p. 97° [from light petroleum (b. p. 60—90°)].

p-2-*Pyridylbenzhydrazide*.—Methyl *p*-2-pyridylbenzoate (3 g.) and hydrazine hydrate (1 c.c.; 100%) were refluxed in ethanol (10 c.c.) for 6 hr. and then cooled. p-2-*Pyridylbenzhydrazide* (1·78 g., 59%) crystallised as glistening plates, m. p. 161·5° (Found: N, 19·8. $C_{12}H_{11}ON_3$ requires N, 19·7%). Some ester (0·74 g., 25%), m. p. 89—94°, was recovered.

N-*Benzenesulphonyl*-N′-p-2′-*pyridylbenzoylhydrazine*.—A mixture of the hydrazide (2·73 g.), dry pyridine (5 c.c.), and benzenesulphonyl chloride (1·77 c.c.) was set aside for 2 days, pyridine removed *in vacuo*, and the residue triturated with dilute ammonia giving the *hydrazine* (4·49 g., 96%) as prisms (from ethanol), m. p. 210° (decomp.) (Found: N, 12·0. $C_{18}H_{15}O_3N_3S$ requires N, 11·9%).

p-2-*Pyridylbenzaldehyde*.—(i) A mixture of the benzenesulphonylhydrazine (1·7 g.), anhydrous sodium carbonate (0·85 g.), and thiosemicarbazide (0·58 g.) in ethylene glycol (5 c.c.) was heated at 160° for 15 min. Dilution with water gave the *thiosemicarbazone* (0·31 g., 25%) as pale yellow microcrystals (from ethanol), m. p. 214—215° (decomp.) (Found: C, 60·65; H, 4·7; N, 21·4. $C_{13}H_{12}N_4S$ requires C, 60·9; H, 4·7; N, 21·85%).

(ii) Sulphuric acid (34 c.c.) was added dropwise with vigorous stirring to a solution of *p*-2-pyridyltoluene (22·4 g.) in acetic acid (230 c.c.) and acetic anhydride (230 c.c.), the temperature being kept below 10°. Chromic acid (40 g.) was added gradually at 5°, and the mixture was then stirred for a further hour below 10° and finally allowed to warm to 30° during 15 min. The viscous green mixture was treated with ice–water (1 l.), neutralised (ammonia solution), and filtered. Extraction of the filtrate gave more solid, the combined solids crystallising from aqueous ethanol as plates, m. p. 103—104°, of p-2-*pyridylbenzaldehyde diacetate* (7·07 g., 19%) (Found: C, 67·05; H, 5·15. $C_{16}H_{15}O_4N$ requires C, 67·35; H, 5·3%). Dilution of the combined mother liquors gave an oil which was purified *via* the bisulphite complex, from which p-2-*pyridylbenzaldehyde* (5·3 g., 20%) was obtained as glistening plates, m. p. 55° (from aqueous alcohol) (Found: C, 78·55; H, 4·95. $C_{12}H_9ON$ requires C, 78·65; H, 4·95%). The 2 : 4-*dinitrophenylhydrazone* formed red needles (from chlorobenzene), m. p. 254—255° (decomp.) (Found: C, 59·35; H, 3·7. $C_{18}H_{13}O_4N_5$ requires C, 59·5; H, 3·6%), and the thiosemicarbazone crystallised from ethanol as cream needles, m. p. 219° (decomp.), undepressed on admixture with the product obtained in (i).

The authors are indebted to Miss B. Stevenson for microanalyses, to Professor S. D. Rubbo for the bacteriological results, and to the National Health and Medical Research Council and the Rockefeller Foundation for financial support.

Organic Chemistry Dept., University of Sydney. [*Received, April 26th*, 1955.]

21. *The Decomposition of Hydrogen Peroxide by Ceric Salts. Part II.* The Action of Ceric Perchlorate.*

By Michael Ardon and Gabriel Stein.

Ceric perchlorate solutions above pH 0·7 may contain a part of the Ce(IV) in the form of a colloidal polymer. Once formed, this polymeric form remains stable in cold 2N-perchloric acid. Solutions containing the polymer yield a coloured complex with hydrogen peroxide which is decomposed only slowly. Such solutions are very much less active photochemically than those containing only $Ce^{4+}_{aq.}$ and its simple products of hydrolysis.

In Part I * it was shown that the reaction between very pure ceric sulphate and hydrogen peroxide in the pH range 0—1·4 was very fast and can be described entirely by the two processes :

$$H_2O_2 + Ce^{4+} \longrightarrow HO_2 + H^+ + Ce^{3+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$HO_2 + Ce^{4+} \longrightarrow O_2 + H^+ + Ce^{3+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Complex formation was not observed. Even if present in large excess and at a high concentration hydrogen peroxide was not attacked by HO_2, and chain reactions did not appear. In these solutions the ceric form is present as sulphate complexes (Moore and Anderson, *J. Amer. Chem. Soc.*, **1945**, **67**, 167). It was observed that in ceric perchlorate solutions, where complex formation is small and the cerium is present as the $Ce^{4+}_{aq.}$ ion and its products of hydrolysis (Hardwick and Robertson, *Canad. J. Chem.*, **1951**, **29**, 818), the reaction with hydrogen peroxide became slow and a coloured complex was formed. In view of the importance of ceric perchlorate solutions in, *e.g.*, photochemical processes, we have now investigated the reaction in perchlorate and nitrate solutions.

Experimental

Solutions were prepared in triply distilled water. The hydrogen peroxide used was of "AnalaR" quality. The ceric solutions were prepared from "AnalaR" quality ceric ammonium nitrate by two methods : (*A*) precipitating ceric hydroxide by ammonia, washing it free from ammonium and nitrate ions, and dissolving it in 2N-perchloric or -nitric acid ("AnalaR") on a water-bath; (*B*) as in (*A*), followed by reduction of the ceric solution thus obtained with hydrogen peroxide and electrolytic reoxidation of the cerous solution. This oxidation was carried out according to Smith, Frank, and Kott (*Ind. Eng. Chem., Anal.*, **1940**, **12**, 268) without a diaphragm.

Dialysis was carried out with regenerated viscose cellulose membranes. Optical density was measured with a Beckman DU spectrophotometer, pH with a Cambridge pH indicator, and redox potentials by means of a Fisher bridge and bright platinum electrodes. Ultraviolet irradiations were by an unfiltered Hanovia S220 lamp as the source.

Results.—When ceric perchlorate solution (0·05—0·1N) prepared according to procedure (*A*) reacted at pH 0—2·0 with hydrogen peroxide solutions, the solution became orange and decomposition of the peroxide was only slow. Fig. 1 shows the absorption spectrum of such a solution and that of the ceric perchlorate solution alone, at the same pH and concentration. The decomposition of the complex may be followed by measuring the optical density at 400 or 425 mμ where the complex has a considerable absorption whilst neither the ceric nor the resulting cerous perchlorate absorbs strongly. As Fig. 2 shows, in one typical experiment, after the initial part where the formation of the complex takes place at a measurable rate, the decomposition is of approximately second order during most of the reaction.

In order to gain information regarding the composition of the complex, measurements by Job's method (Fallab and Erlenmeyer, *Helv. Chim. Acta*, **1953**, **36**, 6) were carried out. Although not entirely satisfactory, owing to the decomposition's taking place during measurements, the results (Fig. 3) indicate a possible simple ratio of $H_2O_2 : Ce^{4+} = 1 : 2$.

When solutions of ceric perchlorate prepared by method (*A*) and capable of giving the complex with hydrogen peroxide were dialysed in a stationary system, it was found that the ceric ions were present mainly in a form which did not pass the membrane. The membrane

* Part I, Baer and Stein, *J.*, 1953, 3176.

FIG. 1.

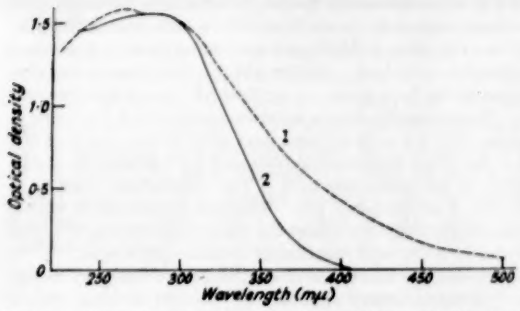

FIG. 2.

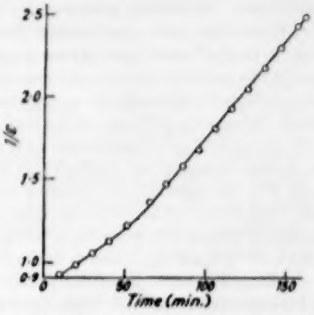

FIG. 1. *Absorption spectrum of ceric perchlorate solution prepared by method (A); (1) in the presence and (2) in the absence of hydrogen peroxide. Both solutions at* pH = 2 *and having* $[Ce^{IV}] = 5 \times 10^{-4}$M, $[H_2O_2] = 0{\cdot}05$M.

FIG. 2. *Decomposition of the complex formed in ceric perchlorate solution [method (A)] on addition of hydrogen peroxide :* 25°, pH = 1·0, $[Ce^{IV}] = 25 \times 10^{-4}$M, $[H_2O_2] = 5 \times 10^{-3}$M.

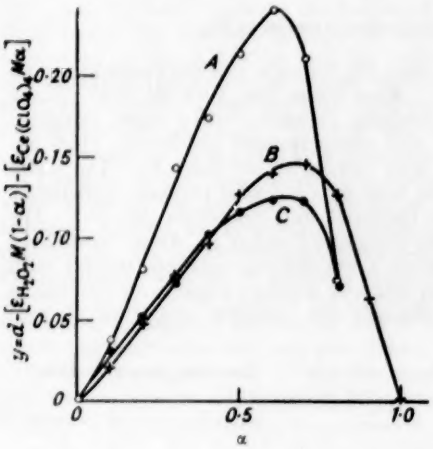

FIG. 3. *Results of using Job's method for the complex between ceric perchlorate [prepared by method (A)] and hydrogen peroxide. Curve A :* M = 1×10^{-3}, $[H^+] = 2 \times 10^{-3}$. *Curve B :* M = $0{\cdot}5 \times 10^{-3}$, $[H^+] = 1 \times 10^{-3}$. *Curve C :* M = $0{\cdot}5 \times 10^{-3}$, $[H^+] = 2 \times 10^{-3}$.

α = mole fraction of ceric ion.

FIG. 4.

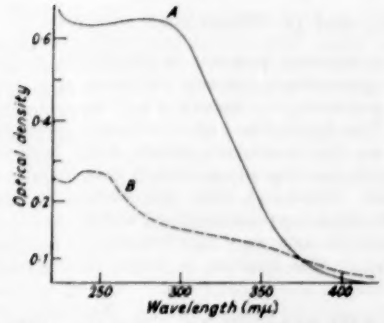

FIG. 5.

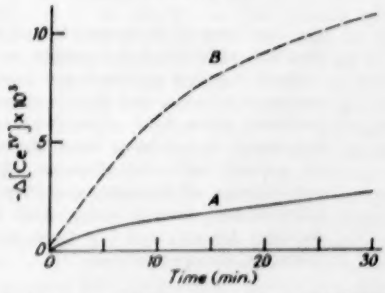

FIG. 4. *Absorption spectra of solutions prepared by methods (A) and (B), obtained with experimental solutions of* 2×10^{-4}M*-concentration in both cases, in* N-$HClO_4$ *solution.*

FIG. 5. *Ultraviolet irradiation of solutions prepared by methods (A) and (B).* Ceric solutions $1{\cdot}5 \times 10^{-4}$M in N-$HClO_4$. Decrease in ceric concentration as function of time of irradiation in minutes.

was slightly attacked chemically and the solution remaining in it gave the reaction with hydrogen peroxide. Solutions prepared by method (*A*) were thermally stable for very long periods.

When the ceric perchlorate solutions were prepared by method (*B*), it was found that in, *e.g.*, 0·1N-Ce^{IV} solutions in the range of pH 0—0·7, they did not give any complex with hydrogen peroxide and the decomposition of the latter was very fast. Above pH 0·7, however, a solution so prepared is metastable and passes into one of the type given by method (*A*) at a rate increasing with increasing pH and increasing [Ce^{IV}]. Reconversion into a solution as obtained by method (*B*) by addition of perchloric acid is possible only for a short time and after some ageing of the solution obtained by method (*A*) [formed either from the solution obtained by method (*B*) above pH 0·7, or directly] it remains stable even in 2N-perchloric acid. The absorption spectra of the two types of solution are compared in Fig. 4 at the same pH. Dialysis experiments with a solution prepared by method (*B*) were unsuccessful since it attacks the membrane strongly, till all the Ce^{IV} is used up; also it decomposes water in a thermal reaction at a measurable rate.

Measurements of potential difference between the two types of solution were made by means of a concentration cell, with agar bridges. Concentrations of total Ce^{IV} (*a*) and of total cerium including cerous (*b*) were determined in both half-cells by (*a*) potentiometric titration with Fe^{2+} in excess of sulphuric acid and (*b*) oxidation with ammonium persulphate followed by potentiometric titration with Fe^{2+} in excess of sulphuric acid. The results showed that the ratio $Ce^{4+}{}_A : Ce^{4+}{}_B$ is not greater than 0·05 when both solutions are in 1N-perchloric acid each containing 0·1N-Ce^{IV} and where Ce^{4+} denotes the species of free hydrated ceric ions with respect to which the electrodes are reversible.

The photochemical stability of the two types of solution is shown in Fig. 5.

Discussion.—The results indicate that in solution (*B*) the ceric ions are present in those forms described by Sherrill, King, and Spooner (*J. Amer. Chem. Soc.*, 1943, **65**, 170). These solutions do not give a complex with hydrogen peroxide, appear to have a higher oxidation potential, and decompose water in thermal and photochemical processes; they are metastable even at relatively low pH values with respect to solution (*A*). The latter appears to contain the ceric ions mainly in the form of a colloidal polymer, apparently related to the dimer $[Ce{-}O{-}Ce]^{6+}$ discussed by Hardwick and Robertson (*loc. cit.*). The formation of such polymers has been assumed by King and Pandow (*J. Amer. Chem. Soc.*, 1952, **74**, 1966). The colloid observed by us gives a well-defined coloured complex with hydrogen peroxide. Once formed and aged the colloidal polymer remains stable even in 2N-perchloric or -nitric acid and strongly influences the chemical properties of such solutions.

Hebrew University, Jerusalem, Israel. [*Received, June 27th*, 1955.]

22. *The Pyrolysis of Organomercury Compounds.*

By H. V. Carter, E. I. Chappell, and E. Warhurst.

The thermal decomposition of diethyl- and diphenyl-mercury, of phenylmercuric chloride and bromide, and of *n*-propylmercuric chloride has been studied in a flow system using low substrate pressures, in presence of a large excess of toluene, and short contact times. The mechanisms of the decompositions have been discussed and values for the activation energy and frequency factor have been obtained for each decomposition except that of *n*-propylmercuric chloride. It has been concluded that the data available for all the organomercury compounds which have been studied so far fall into two distinct classes with regard to activation energy and frequency factor. An attempt has been made to explain this division in terms of potential-energy surfaces.

Although previous work [Gowenlock, Polanyi, and Warhurst, (I) *Proc. Roy Soc.*, 1953, *A*, **218**, 269; Chilton and Gowenlock, *Trans. Faraday Soc.*, 1953, **49**, 1451; 1954, **50**, 824; Laurie and Long, *ibid.*, 1955, **51**, 665] on the thermal decomposition of mercury alkyls has

not covered a wide field, the results obtained so far fall into two groups with regard to activation energy and frequency factor (see Table 2).

On the one hand is dimethylmercury, for which the activation energy of the homogeneous decomposition is undoubtedly less than the sum of the first and the second mercury–carbon bond-dissociation energies as determined by Mortimer, Pritchard, and Skinner (*ibid.*, 1952, **48**, 220) and by Carson, Carson, and Wilmshurst (*Nature*, 1952, **170**, 320) from thermochemical studies. There can be little doubt that in this case the activation energy can be accepted as a reliable figure for the dissociation energy, D_1, of the first mercury–carbon bond, *i.e.*, D(AlkHg–Alk). That, on this basis, the dissociation energy, D_2, of the second bond is much smaller than D_1, has been explained by Gowenlock, Polanyi, and Warhurst (II) (*Proc. Roy. Soc.*, **1953**, *A*, **219**, 270). The frequency factor, ν, for the decomposition of dimethylmercury is about 3×10^{13}. Values of $\sim 10^{13}$ have been found for numerous bond-dissociation reactions by Szwarc and his collaborators (*Chem. Rev.*, **1950**, **47**, 75) and are sometimes referred to as a " normal " frequency factor for a unimolecular reaction.

On the other hand, there are di-*n*- and di*iso*-propylmercury (Chilton and Gowenlock, *Trans. Faraday Soc.*, **1953**, **49**, 1451; **1954**, **50**, 824), for which the activation energies of the first-order decomposition are approximately equal to the *sum* of the first and the second dissociation energies (*i.e.*, to $D_1 + D_2$) and certainly larger than any plausible value of D_1. Also, for both reactions the frequency factor is in the range 10^{15}—10^{16}, at least 100 times larger than the so-called normal value. Chilton and Gowenlock, on the basis of a suggestion by Peard, Stubbs, and Hinshelwood (*Proc. Roy. Soc.*, 1952, *A*, **214**, 471) concerning the decomposition of certain hydrocarbons, consider that in the decomposition of these two mercury alkyls the activation energy is not localised in one bond but in both mercury–carbon bonds and the first step is assumed to be $Hg(Alk)_2 \longrightarrow Hg + 2Alk$, *i.e.*, the molecule breaks into *three* fragments.

The present work was initially a continuation of the work on dimethylmercury with a view to extending the determinations of mercury–carbon bond-dissociation energies. However, Chilton and Gowenlock's results for di-*n*- and di*iso*-propylmercury and our own observations on diphenylmercury showed that this aspect of pyrolytic work was limited. It appeared to us that, in addition to the amassing of further data on bond-dissociation energies, an extensive study of the pyrolysis of compounds of the types R_2Hg and RHgX, where R is an alkyl or aryl radical and X is a halogen atom, would be of interest in substantiating whether or not only two distinct types of behaviour are exhibited with regard to thermal decomposition. It was also considered that such an investigation might reveal connections between differences in behaviour and factors such as structural and energetic differences in the molecules.

Experimental

Preparation and Purification of Materials.—Diethylmercury, from Messrs. Light and Co. Ltd., was dried and fractionated under reduced pressure in an efficient column packed with stainless-steel gauze. The fraction collected between 46·0° and 46·3°/11 mm. was used in the pyrolysis experiments. Diphenylmercury (B.D.H.) was slowly sublimed in a good vacuum at a temperature just below its m. p. The middle sublimation fractions melted sharply at 124°. Phenylmercuric chloride and bromide and *n*-propylmercuric chloride were prepared by the same method, *viz.*, by mixing equimolar amounts of HgR_2 and HgX_2 in a suitable solvent. The precipitated RHgX was washed and recrystallised and then dried by thorough pumping *in vacuo*. The products melted sharply at 251°, 276°, and 145°, respectively. The di-*n*-propylmercury required for the preparation of *n*-propylmercuric chloride was prepared by Gilman and Brown's method (*J. Amer. Chem. Soc.*, **1930**, **52**, 3314). The carrier gases, nitrogen and carbon dioxide (which was used in a few experiments only), were purified by slow passage through sodium vapour at 350°. The toluene was a special "sulphur low" product from Messrs. Hopkin and Williams Ltd. It was purified by " pre-pyrolysis " twice at 900°, followed by distillation in an efficient column.

Apparatus.—The apparatus used was that described by Gowenlock, Polanyi, and Warhurst (I) (*loc. cit.*). It consisted essentially of a circulation system through which nitrogen could be

streamed at known pressures and known rates of flow. Immediately after leaving the circulation pump the nitrogen was completely freed from mercury (from the pump) by a U-tube system in which the gas was several times alternately heated to 200° and cooled to −195°. The flow was then split into two calibrated branches—a toluene branch, *T*, and a substrate branch, *S*. Toluene vapour was introduced into the carrier gas in *T*, and substrate vapour in *S*. The two streams then united and passed through the hot reaction vessel, after which the gases passed through a U-tube at 0° in which mercury, dibenzyl, and various other products, depending on the substrate investigated, were collected. The toluene was condensed out in a trap at −80° immediately after the U-tube, and a further trap at −195° ensured the removal of all volatile products with the exception of methane (if any) from the nitrogen stream. Before returning to the circulation pump, the nitrogen passed through a calibrated capillary across a double McLeod gauge for measurements of the rate of flow. Known vapour pressures (1—4 mm.) of toluene were maintained in the reaction vessel by saturating the nitrogen stream in branch *T* with the vapour from liquid toluene at a known temperature. A similar technique was used in branch *S* for substrate vapour pressures.

The method of analysis of the products which were condensed out in the U-tube varied with each compound investigated. For the experiments with diethylmercury in the presence of toluene, mercury, possibly with traces of dibenzyl, was the only condensate. The U-tube was rinsed with ether several times to remove dibenzyl, and the mercury determined by direct weighing. For experiments in which toluene was absent the rinsing process was omitted. In the pyrolysis experiments with compounds PhHgX (X = Cl or Br), which were all carried out in the presence of toluene, the possible products in the U-tube are mercury, dibenzyl, diphenyl, mercurous halide, and unchanged PhHgX. The U-tube was washed several times with boiling toluene, rinsed with ether, dried, and weighed. This extraction removes dibenzyl, diphenyl, and PhHgX. The residue was then treated with hot potassium iodide solution, and the U-tube rinsed with water, acetone, and ether, dried, and re-weighed. This treatment converts mercurous halide into a soluble complex and liberates half the mercury as free metal. The total free mercury which remained in the U-tube was determined by direct weighing. These weighing give the separate amounts of mercury and Hg_2X_2. In experiments with Ph·HgCl the above procedure showed that, in the conditions used, the amounts of mercurous chloride were a very small fraction of the total mercury in the products. Consequently, for increased speed of working, the treatment with potassium iodide could be omitted without incurring significant errors in the velocity-constant determinations. For *n*-propylmercuric chloride the full analytical method described above was applied, except that acetone was used instead of toluene for the preliminary extraction. The reliability of the various extraction processes was checked by blank experiments.

Volatile products, such as certain hydrocarbons and hydrogen chloride and bromide, were estimated by pumping the gases from the main apparatus into an analytical section in which the pressures exerted by each gas in a calibrated volume space could be measured. In many cases the process of transferring the various volatile fractions to the analytical section involved careful selective refrigeration of the trap in the main apparatus from which the products were being distilled. The degree of unsaturation of hydrocarbon fractions was determined in the analytical section by Robb and Melville's technique (*Proc. Roy. Soc.*, 1949, *A*, **196**, 445), and in a few experiments also by absorption of the unsaturated hydrocarbons in concentrated sulphuric acid containing silver sulphate (Gooderham, *J. Soc. Chem. Ind.*, 1938, **57**, 388): the two methods gave results in reasonable agreement.

Two methods were used for the determination of the amounts of hydrogen halides produced. In some experiments the gas was pumped from the main apparatus to the analytical section, and its pressure measured. For fractions in which the hydrogen halide could not be easily separated from hydrocarbons, the drop in pressure on absorption of the halide by saturated aqueous potassium hydroxide was measured. The other method consisted in distilling the hydrogen halide into a side trap in the main apparatus in which the contents could then be dissolved in water and the acid determined by the liberation of iodine from iodide–iodate solution. We are not satisfied with either of these methods. Compared with our mercury and hydrocarbon determinations, the results were not very reproducible and we have only used them in a qualitative way in our Discussion.

Most of the pyrolyses were carried out within the following range of experimental conditions: total pressure in reaction vessel = 10 ± 1 mm.; time of contact = 0·1—0·3 sec.; decomposition = 10—75%; substrate pressure in reaction vessel = 1—10 × 10^{-2} mm.; and (toluene/substrate) ratios in the reaction vessel of 30—200. A typical set of results at one temperature

TABLE 1.

Compound	Temp.	$100P_{substrate}$ (mm.)	$\frac{P_{toluene}}{P_{substrate}}$	τ (sec.)	Decompn. (%) † I	Decompn. (%) † II	Vel. const., k (sec.$^{-1}$)
Ph·HgCl	703°	4·15	47	0·190	12·2	—	0·683
	703	4·48	43	0·202	16·0	—	0·859
	703	4·08	47	0·244	17·1	—	0·766
$HgPh_2$	658	1·31	140	0·161	20·0	—	1·39
	658	1·41	136	0·145	18·3	—	1·40
	658	2·51	77	0·401	38·6	—	1·22
	658	3·53	54	0·444	42·1	—	1·23
	658	1·11	173	0·142	15·5	—	1·19
$HgEt_2$	370	12·0	*	0·351	19·9	26·8	0·633
	370	12·0	*	0·317	17·7	17·7	0·616
	370	12·0	*	0·365	20·4	20·1	0·621
	370	9·0	34	0·303	15·6	15·2	0·552
	370	9·0	34	0·296	18·2	16·6	0·646
	370	9·0	32	0·225	12·5	13·2	0·613
Ph·HgBr	701	6·29	46	0·267	41·8	—	2·00
	702	3·34	81	0·168	28·3	—	1·98
	702	5·33	51	0·275	39·7	—	1·84
Pr^n·HgCl	564	4·82	89	0·142	10·6	18·3	0·79
	564	5·50	79	0·140	11·7	17·2	0·89
	565	8·27	52	0·182	24·6	17·4	1·55
	563	13·8	31	0·126	27·2	26·5	2·53

* Toluene absent.

† The figures for the percentage decomposition for Ph·HgCl, $HgPh_2$, and $HgEt_2$ given in the column labelled I are based on the yield of mercury; those for Ph·HgBr and Pr^n·HgCl are based on the yield of ($Hg + 2Hg_2X_2$). The figures for the percentage decomposition given in the column labelled II are based on the yield of ($C_4 + \frac{1}{2}C_2$) for $HgEt_2$ and on ($\frac{1}{2}C_1 + \frac{1}{2}C_2 + C_3$) for Pr^{n}HgCl.

for each compound is shown in Table 1. The velocity constants have been calculated from $k = (1/\tau) \ln 100/(100-f)$, where τ is the time of contact in seconds, and is equal to

$$\frac{\text{Effective volume of reaction vessel}}{\text{Volume flow through reaction vessel}}$$

and f = the percentage decomposition = $100P/S$, where S and P are the number of moles of substrate and relevant product which pass through the reaction vessel during the time of the experiment. For diethylmercury values of f were calculated both from the weight of mercury and from the yield of $C_4H_{10} + \frac{1}{2}(C_2H_6 + C_2H_4)$, which were the only hydrocarbon products. Velocity constants were calculated from the mean of the two values for f. For diphenylmercury and phenylmercuric chloride the values of f were calculated from the mercury yield. As mentioned above, the fact that, in the latter case, a very small fraction of the weighed product was mercurous chloride could be ignored. The f values for phenylmercuric bromide and propylmercuric chloride were based on the yields of $Hg + 2Hg_2X_2$. In connection with the values of f for the last two compounds and phenylmercuric chloride, it should be emphasised that, because of the large atomic weight of mercury, the values of k are very insensitive to relatively large errors in the determination of the *proportions* of mercury and mercurous halide in the products.

For all the compounds investigated, except *n*-propylmercuric chloride, the kinetics were of the first order in substrate concentration. Changes in substrate concentration and in the time of contact over a range of 2—4-fold produced no significant drift in the values of k (for some examples, see Table 1). Figs. 1 and 2 show the results as Arrhenius plots of log k against $1/T$. Two sets of results are shown for diphenylmercury. The dotted circles and dotted line correspond to some early experiments. By comparing the results of substrate vapour-pressure calibrations at the end of this series with those at the beginning, it was found that the degree of saturation of the carrier gas stream in the S branch had decreased considerably. The sequence of runs started at the lowest temperature and worked progressively up to the highest. As a consequence, although the data cannot provide an accurate value for the activation energy, they give, unambiguously, a lower limit of $\sim$ 63 kcal. for this quantity. The full circles and straight line correspond to experiments in which the above defect was eliminated and we attach more importance to these results.

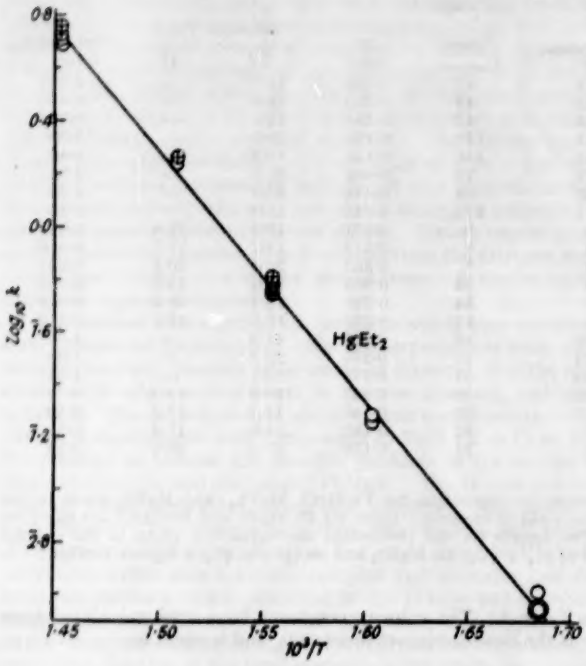

FIG. 1.

○, *Toluene absent.*
⊕, *Toluene/substrate ratio, ~30.*

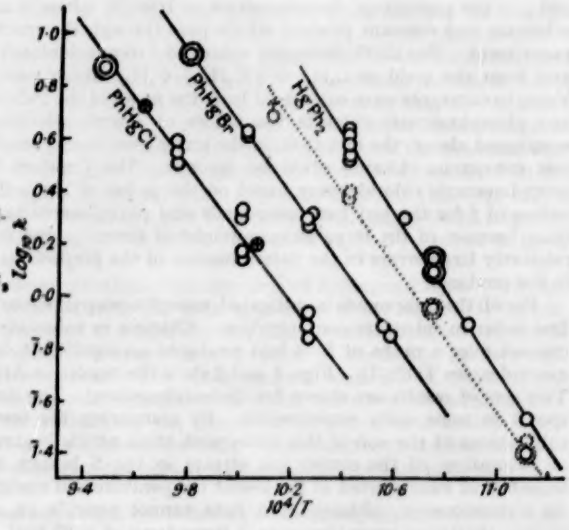

FIG. 2. *Toluene present in all experiments.*

⊕ *includes the small amount of* Hg_2Cl_2 *in the product.*

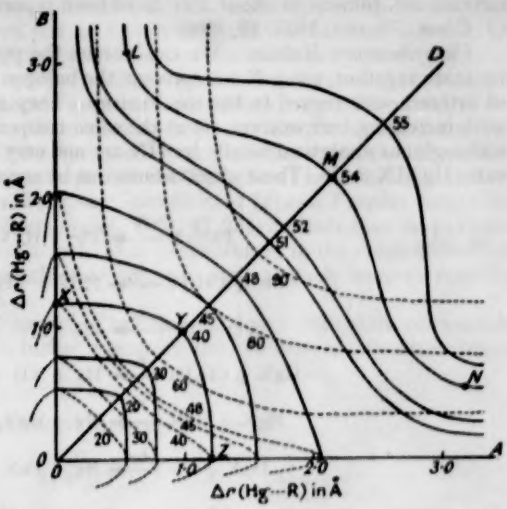

FIG. 3.

(*Contours in kcal. mole*$^{-1}$.)

DISCUSSION

Reaction Mechanisms.—The apparatus was not designed for detailed determinations of all the products in each of the thermal decompositions studied. This is not necessary for the determination of velocity constants. Nevertheless, plausible mechanisms can be suggested in most cases, and supported, in some instances, by a certain amount of experimental evidence.

Diethylmercury.—The general features of this pyrolysis in the absence of toluene were as follows. The only hydrocarbons produced in any appreciable quantities were ethane, ethylene, and butane. The ratios ethane/ethylene ($\approx$1) and C_4/C_2($\approx$4) were both practically independent of temperature. These rough observations are in agreement with the more detailed and accurate work of Ivin and Steacie (*Proc. Roy. Soc.*, 1951, *A*, **208**, 25) on the photolysis of diethylmercury. There can be little doubt that the principal reactions involved are :

$$(C_2H_5)_2Hg \xrightarrow{k_1} C_2H_5Hg + C_2H_5 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$C_2H_5Hg \xrightarrow{k_2} C_2H_5 + Hg \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$C_2H_5 + C_2H_5 \xrightarrow{k_3} C_4H_{10} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and

$$C_2H_5 + C_2H_5 \xrightarrow{k_4} C_2H_4 + C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Of these reactions, (3) and (4) have nearly the same activation energy (Ivin and Steacie find $E_4 - E_3 \sim 0{\cdot}8$ kcal. mole^{-1}). For reasons given below we believe this molecule to belong to the same class as dimethylmercury, the first step in the thermal decomposition being a dissociation into two fragments. Application of the stationary-state method to the above mechanism gives :

$$d[C_4 + \tfrac{1}{2}C_2]/dt = d[Hg]/dt = k_2[C_2H_5Hg] = k_1[Hg(C_2H_5)_2]$$

It can be seen from the Arrhenius plot shown in Fig. 1 that the presence of toluene, at concentrations more than 30 times that of the substrate, has no effect on the velocity constant. It was also found to have only a very minor effect on the hydrocarbon composition. This indicates that the reaction between ethyl radicals and toluene at about 350° is slower than reactions (3) and (4). Similar observations with regard to methyl

radicals and toluene at about 250° have been reported by Murawski, Roberts, and Szwarc (*J. Chem. Physics*, 1951, **19**, 698).

Phenylmercury Halides.—We can discuss the pyrolysis of phenylmercuric chloride and bromide together, using X to represent the halogen atom. There are three general aspects of interest with regard to the mechanism. They are: (*a*) the ratio Hg/Hg_2X_2 increases with increasing temperature, (*b*) at the same temperature $Hg/Hg_2Cl_2 > Hg/HgBr_2$, and (*c*) although our analytical results for HX are not very satisfactory, there is no doubt that the ratio $Hg/HX > 1$. These observations can be accounted for by the following mechanism:

$$PhHgX \xrightarrow{k_5} Ph\cdot + HgX\cdot \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$Ph\cdot + CH_3Ph \xrightarrow{k_6} PhH + \cdot CH_2Ph \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$Ph\cdot + Ph\cdot \xrightarrow{k_7} Ph_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$HgX + CH_3Ph \xrightarrow{k_8} Hg + XH + \cdot CH_2Ph \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$HgX + HgX \xrightarrow{k_9} Hg + HgX_2 \xrightarrow[\text{exit tube}]{\text{In the cold}} Hg_2X_2 \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$HgX + Ph\cdot \xrightarrow{k_{10}} Hg + PhX \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

There are a number of possibilities for the fate of the HgX radical. We have rejected the dissociation of HgX, by either a unimolecular or a bimolecular (*i.e.*, by collision with toluene or nitrogen molecules) process since, in order to account for the appearance of Hg_2X_2 in the products, it would be necessary to postulate that some X atoms escaping reaction emerged from the reaction vessel. This is exceedingly unlikely in view of the relatively large pressure of toluene with which it is known that both chlorine and bromine atoms react extremely rapidly (see, *e.g.*, Anderson, Scheraga, and Van Artsdalen, *J. Chem. Physics*, 1953, **21**, 1258; Szwarc and Williams, *Proc. Roy. Soc.*, 1953, *A*, **219**, 353; Pritchard, Pyke, and Trotman-Dickenson, *J. Amer. Chem. Soc.*, 1955, **77**, 2629; Szwarc and Taylor, *J. Chem. Phys.*, 1954, **22**, 270). We have chosen reaction (9) to account for the presence of Hg_2X_2 in the products since, for both X = Cl and Br, the reaction is more than 50 kcal. $mole^{-1}$ exothermic and would be expected to be very fast with a negligible activation energy. Reaction (8) is regarded as the main mercury-producing reaction and is about 1 kcal. exothermic and 7 kcal. endothermic for X = Cl and Br, respectively. It is not unreasonable to expect, therefore, activation energies of 5—10 kcal. $mole^{-1}$ for the chloride and 10—15 for the bromide. These values, together with the high concentration of toluene, would explain why reaction (8) is able to compete effectively with reaction (9). The assumption that $E_8 > E_9$ accounts for the increase in the Hg/Hg_2X_2 ratio with increase in temperature. The assumption that E_8 (X = Br) $> E_8$ (X = Cl) while $E_9 \simeq 0$, for both X = Cl and Br, would account for the fact that $Hg/Hg_2Br_2 < Hg/Hg_2Cl_2$ for a given temperature. Reaction (10) accounts for the fact that the ratio Hg/HX is greater than unity. Application of the stationary state method to the mechanism gives:

$$d[Hg + 2Hg_2X_2]/dt = k_8[HgX][PhCH_3] + k_{10}[Ph][HgX] + 2k_9[HgX]^2 = k_5[PhHgX]$$

Diphenylmercury. We did not attempt to determine the hydrocarbon products of the pyrolysis of this compound. It is extremely probable that the mechanism is:

$$HgPh_2 \xrightarrow{k_{11}} Hg + 2Ph\cdot \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$Ph\cdot + Ph\cdot \xrightarrow{k_{12}} Ph_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$Ph\cdot + CH_3Ph \xrightarrow{k_{13}} PhH + \cdot CH_2Ph \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

For reasons given later, we consider that the first step in the decomposition breaks both Hg–C bonds and gives three fragments.

n-Propylmercuric chloride. Decomposition of this was much more complex than that of the other molecules studied; it was not of first order in substrate concentration (see Table 1) and the mechanism involves chain reactions. The nature of the hydrocarbon products showed that nearly all the propyl radicals produced decomposed into methyl radicals and ethylene. The chain reaction (or reactions) probably involves attack of the substrate by methyl radicals. It was not possible to derive a value for activation energy from our results. We think that this complexity will very probably apply to all molecules of the type AlkHgX, with the possible exceptions of CH_3HgX. The Alk–HgX dissociation energy values given by Mortimer, Pritchard, and Skinner (*Trans. Faraday Soc.*, 1952, **48**, 220) and Hartley, Pritchard, and Skinner (*ibid.*, 1951, **47**, 254) indicate that the pyrolysis of these compounds would necessitate relatively high temperatures, in the range 650—750°. Our experience with *n*-propylmercuric chloride suggests that at such temperatures the kinetics would not be straightforward.

Activation Energies and Frequency Factors.—The value of E * and ν for the decompositions which we have studied, together with earlier examples and the relevant thermochemical data, are collected in Table 2.

TABLE 2. (All energies in kcal. mole^{-1}.)

Molecule	$D_1 + D_2$	D_1	D_2	E	log ν
$HgMe_2$	57·3 ± 4 [a]	51·5 ± 2	~6	51·5 ± 2 [e]	13·5 [e]
	57·1 ± 2 [b]			51·3 ± 0·5 [d]	14·3 [d]
$HgEt_2$	45·1 ± 6 [a]	42·5 ± 2	~5	42·5 ± 2	14·1
	48·5 [a]				
PhHgCl	(81·6 ± 3) [c]	(58·6 ± 3)	23	59 ± 3	13·0
	85·8 ± 3 [c]	62·8 ± 3 [c]			
PhHgBr	(75·7 ± 3) [c]	(58·7 ± 3) [c]	17	63 ± 2	14·3
	79·9 ± 3 [c]	62·9 ± 3 [c]			
$HgPh_2$	(55·4 ± 9) [f]	—	—	68 ± 4	16·0
	63·8 ± 9			>63	
$HgPr^n_2$	49·4 ± 4 [a]	—	—	46·5 [g]	15·3 [g]
$HgPr^i_2$	40·3 ± 7 [a]	—	—	40·4 ± 1 [h]	16·7 [h]

[a] Mortimer, Pritchard, and Skinner, *Trans. Faraday Soc.*, 1952, **48**, 220. [b] Carson, Carson, and Wilmhurst, *Nature*, 1952, **170**, 320. [c] Gowenlock, Polanyi, and Warhurst, *Proc. Roy. Soc.*, 1953, *A*, **218**, 269. [d] Laurie and Long, *Trans. Faraday Soc.*, 1955, **51**, 665. [e] Pritchard, Thesis, Manchester, 1951. [f] Hartley, Pritchard, and Skinner, *Trans. Faraday Soc.*, 1951, **47**, 254. [g] Chilton and Gowenlock, *ibid.*, 1954, **50**, 824. [h] *Idem, ibid.*, 1953, **49**, 1451.

The figures given in parentheses for Ph·HgCl, Ph·HgBr, and $HgPh_2$ are based on D(Ph–H) = 97·8 kcal. [see ref. (*e*)]; the corresponding figures without parentheses are based on D(Ph–H) = 102 kcal.

The results for phenylmercuric chloride and bromide show that the pyrolytic method can yield good values for D_1. The agreement between our values of E and Pritchard's values of D_1 (Thesis, Manchester, 1951) from thermochemical measurements is as good as can be expected. It was merely a very reasonable inference by Gowenlock, Polanyi, and Warhurst (I) (*loc. cit.*) that their value of 51·5 for the activation energy of decomposition of dimethylmercury was a good value for D_1. The results for phenylmercuric chloride and bromide strengthen this inference considerably. Our results for diethylmercury now firmly establish the activation energy for this decomposition as 42·5 ± 2 kcal. mole^{-1}, and since this is appreciably lower than the probable thermochemical value for $D_1 + D_2$, we believe that it is a good value for D_1. The earlier figure of 41·5 given by Gowenlock, Polanyi, and Warhurst (I) (*loc. cit.*) was based on the assumption that the frequency factors for the decompositions of dimethyl- and diethyl-mercury were identical.

We consider that the data given in Table 2 for the seven organomercury compounds studied so far substantiate the suggestion that each compound belongs to one or other of two distinct classes with regard to its behaviour on thermal decomposition. Class I, which consists of $HgMe_2$, $HgEt_2$, PhHgCl, and PhHgBr, is characterised by $D_1 + D_2 > E = D_1$

* The values given in the Table for the compounds we have investigated have been derived as follows. The method of least squares has been applied to each set of data and the value of E obtained from the resulting slope has been decreased by 0·5 kcal. to allow for the fact that the velocity constants at the lower end of the temperature range are less accurate than at the higher end, the likely errors being such as to make the low-temperature constants too small.

and $\log \nu = 13{\cdot}7 \pm 0{\cdot}7$, *i.e.*, frequency factors in the so-called " normal " range. Class II consists of $HgPr^n_2$, $HgPr^i_2$, and $HgPh_2$ and is characterised by $E \approx D_1 + D_2$ and $\log \nu = 16 \pm 0{\cdot}7$. This important feature merits further discussion. Consider class II: if these decompositions actually involved the breaking of only one bond, then it would be necessary to assume that phenyl, *iso*propyl, and *n*-propyl groups, for some reason, caused the potential-energy curve for the bond dissociation to possess a hump, the height of which happened to be equal to the particular value of D_2 in each case. This seems extremely unlikely and we adopt the view that this class of compound decomposes into three fragments in one step, the activation energy being identified with $D_1 + D_2$. We also consider it very unlikely that this characteristic of class II arises because the values of D_2 are zero. Of all the examples of HgR radicals, it would be expected that HgPh would possess the strongest bond because of the possibility of conjugation involving orbitals of the mercury atom and the π electrons of the benzene ring. Turning to class I, it seems evident that the main reason why the first step in the dissociation of phenylmercuric chloride and bromide involves the rupture of one bond only is because D_2 for these two cases is relatively large. Increases in activation energy of 23 and 17 kcal. mole^{-1}, respectively, are probably too large to be offset by increases in frequency factor. However, the size of D_2 cannot be the sole cause for the division into two classes, since dimethylmercury, which dissociates into two fragments, almost certainly has a value of D_2 which is smaller than that for diphenylmercury.

Dissociation of the molecule HgR_2 into three fragments clearly causes a change from the bivalent to the zero-valent state in the mercury atom. Gowenlock, Polanyi, and Warhurst (II) (*loc. cit.*) have shown that this also occurs when the molecule dissociates into two fragments, Hg^0R and R, and that this is responsible for the striking feature in the thermochemistry of the mercury alkyls, *viz.*, that $D_1 + D_2$ is only a little larger than D_1. It is of some interest to examine the detailed energetics of the two possible modes of decomposition. Fig. 3 shows two potential-energy surfaces for configurations of the HgR_2 molecule. The first, drawn in broken curves, depicts the situation when the two Hg–R bonds in the molecule are *completely independent of each other*. The relevant potential-energy curve applicable to extensions of either of the two bonds was assumed to be the Morse function $V = 50[1 - \exp(-1{\cdot}87\Delta r)]^2$, where V is the potential energy relative to the unstretched state as zero, Δr is the bond extension, and the Morse constant $a = 1{\cdot}87$ has been derived from the value of the force constant ($2{\cdot}4 \times 10^5$ dynes cm.$^{-1}$) calculated by Thompson and Linnett (*Proc. Roy. Soc.*, 1937, *A*, **160**, 593) for the bonds in dimethylmercury. A typical value of 50 kcal. has been chosen for the energy of dissociation of either of the two bonds. This first energy surface is obtained when it is assumed that the above Morse curve applies to extensions of one of the mercury–carbon bonds *irrespective of the state of extension of the other*. This means that the dissociation energy of the HgR radical is also 50 kcal. This surface, which is very similar to that constructed by Goodeve (*Trans. Faraday Soc.*, 1934, **30**, 60) for the carbon dioxide molecule, consists of two valleys (each parallel to a co-ordinate axis) and a high plateau. Dissociation into two fragments corresponds to moving up one or other of the valleys from O (the ground state of the molecule) to A or B, with an increase in potential energy of $D_1 = 50$ kcal. Dissociation into three fragments corresponds to moving from O to D on the plateau, with an increase of potential energy of $2D_1$, *i.e.*, 100 kcal., the path along the diagonal being much steeper than that along the valleys. In these circumstances the molecule HgR_2 would clearly dissociate into two fragments with $E = D_1$. Further, the molecule being considered as a three-particle system, it is clear that only the unsymmetrical mode of vibration ν_3 will be relevant. On these grounds a frequency factor of $\sim 10^{13}$ might be expected.

The second potential-energy surface, drawn in full curves, represents an attempt to describe approximately the state of affairs for a " real " mercury alkyl, which differs from the above case in two important aspects, *viz.*, (*a*) that $D_1 + D_2 = D_1 + 6$, which gives a very low plateau, and (*b*) that the two bonds are not energetically independent. For example, in the simultaneous, symmetrical stretching of the molecule the dissociation limit for *each* bond must now be $(D_1 + D_2)/2$, *i.e.*, 28 kcal. and not 50 kcal., as for the first

surface. The full details of this bond interdependence are extremely difficult, if not at present impossible, to assess. We have attempted to deal with it for symmetrical stretched configurations only, *i.e.*, for points on the diagonal of the potential-energy surface. For these we have assumed that the Morse constant of 1·87 still applies, *i.e.*, that the energy of a point on the diagonal is given by $V = 2 \times 28[1 - \exp(-1{\cdot}87\Delta r)]^2$. The energy changes for stretching one bond only, *i.e.*, moving from O to A or B, are again given by the expression $V = 50(1 - \exp -1{\cdot}87\Delta r)^2$. For total energies in the region $56 > V > 50$, we need the potential curve for the dissociation of the "real" HgR radical. We have used the Morse function $V = 6[1 - \exp(-a\Delta r)]^2$ for this, the constant a being derived from the force constant of the very similar molecule, HgH. The exact shape of this curve is of minor importance in our discussion. Our method of plotting the second energy surface, using the above three Morse functions, thus gives us only three points per energy contour, *e.g.*, X, Y, Z for $50 > V > 0$ and L, M, N for $56 > V > 50$, and, to obtain merely the general features of the surface, we have sketched the contours very roughly from these points, utilising, of course, a number of obvious trends which the contours must follow, for example, as they approach very large values for one of the bond lengths.

The second surface shows a striking contrast to the first in that the two distinct valleys have vanished, leaving a broad shallow basin, symmetrical about the diagonal.* We believe that this aspect is probably real and does not arise from the crudity of our methods. The important configurations are actually those on the diagonal, and it does not appear likely that the uncertainties in the assumed potential function for these configurations could be solely responsible for the disappearance of the two valleys. This basin-like form of the second surface has the consequence that the difference in steepness between the diagonal path OD and the paths OA and OB is much less than that for the first surface, *i.e.*, dissociation into three fragments becomes relatively much more likely. Further, for configurations represented by points in the basin near the diagonal, it is clear that more than one fundamental mode of vibration is important for the dissociation into three fragments; the symmetrical modes ν_1 and the doubly degenerate ν_2 are all relevant. On these grounds it is reasonable to expect an increased frequency factor for this type of decomposition. We suggest tentatively that the precise details of the membership of the various organomercury compounds in the two classes of behaviour may depend very sensitively on the curvature of the basin-like surface in the region of the diagonal, and that for members of class II the basin-like character may have become so pronounced that the diagonal path is actually less steep than the OA or OB paths, whereas for class I this is not so. One of the important factors which affects the curvature of the surface in this region is the following. In the unstretched state, the molecule can be represented by the valency-bond configuration R–Hg^{II}–R, with very little contribution from the structure R–Hg^{0}–R, in which the mercury atom is zero-valent. When the molecule is stretched the contribution of the latter structure increases at the expense of the former. This is the most important factor which is responsible for the interdependence of the two bonds in the molecule. With two different organomercury compounds, there may be appreciable differences in the rate at which the contribution of the zero-valent structure increases when the bonds are stretched and this would produce differences in the curvature of the energy surfaces.

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THE UNIVERSITY, MANCHESTER, 13. [*Received, July 8th*, 1955.]

* We have rejected the possibility that the surface consists of *three* valleys (one along each of the co-ordinate axes and one along the diagonal) for the following reason. If one of the bonds were stretched to an extent corresponding to the point X, say, in Fig. 3, then on stretching the other bond, corresponding to moving from X in a direction parallel to OA, it is found that this extension curve would possess at least *two* points of inflexion. We consider that this is extremely unlikely; a normal bond extension curve only possesses *one* point of inflexion.

23. *The Addition of Thiolacetic Acid to Ethynylcarbinols and the Conversion of the Adducts into Aldols and αβ-Unsaturated Aldehydes.*

By Henry Bader.

"Abnormal" addition (cf. *J.*, 1949, 619) of thiolacetic acid to α- and β-ethynylcarbinols produces hydroxyalkenyl thiolacetates or alkadienyl thiolacetates (R·CH:CH·CH:CH·SAc) and diacetylthioalkanols. The monoadducts are converted by the usual carbonyl reagents into derivatives of the corresponding aldols or αβ-unsaturated aldehydes, while under the same conditions the dienyl thiolacetates yield the derivatives of αβ-unsaturated aldehydes.

Bader, Cross, Heilbron, and Jones (*J.*, 1949, 619; cf. Behringer, *Annalen*, 1949, **564**, 219) described the addition of thiolacetic acid to monosubstituted acetylenic hydrocarbons alone and under the influence of organic peroxides or irradiation with ultraviolet light. The addition was shown to proceed "abnormally," yielding mono- and di-adducts (I) and (II). The monoadducts were converted by the usual carbonyl reagents into the derivatives of the corresponding saturated aldehydes, while the diadducts under similar conditions yielded 1 : 2-dithiols. Simple adducts of thiolacetic acid and conjugated vinylacetylenes could not be obtained. Consequently, in pursuit of an alternative route to αβ-unsaturated aldehydes, attention was turned to the addition reaction with the readily available ethynylcarbinols. Rearrangement of the latter by formic acid (Rupe and

$$\underset{\text{(I)}}{R\cdot CH{:}CH\cdot SAc} + 2NH_2\cdot NH\cdot CO\cdot NH_2 \longrightarrow R\cdot CH_2\cdot CH{:}N\cdot NH\cdot CO\cdot NH_2 + Ac\cdot NH\cdot NH\cdot CO\cdot NH_2 + H_2S$$

$$\text{(II)}\quad R\cdot CH(SAc)\cdot CH_2\cdot SAc \longrightarrow R\cdot CH(SH)\cdot CH_2\cdot SH$$

Kambli, *Helv. Chim. Acta*, 1926, **9**, 672; 1928, **11**, 449; Rupe and Kuenzy, *ibid.*, 1931, **14**, 708), originally claimed to yield αβ-unsaturated aldehydes, was finally proved to give mostly unsaturated ketones with only traces of the aldehydes (Chanley, *J. Amer. Chem. Soc.*, 1948, **70**, 244; see also McGregor, *ibid.*, p. 3953, and Bergmann, *ibid.*, 1951, **73**, 1218, for special cases where appreciable conversion into the aldehyde did occur). A more indirect, but for the time being the only practical, route for the conversion of ethynylcarbinols into αβ-unsaturated aldehydes is the sequence of reactions employed by Dimroth (*Ber.*, 1938, **71**, 1333, 1346), which however is limited to tertiary α-ethynylcarbinols.

In the present approach a monoadduct resulting from the addition of thiolacetic acid to an α-ethynylcarbinol is hydrolysed to the corresponding aldol which can be easily

$$>C(OH)\cdot C{:}CH \longrightarrow >C(OH)\cdot CH{:}CH\cdot SAc \longrightarrow >C(OH)\cdot CH_2\cdot CHO \longrightarrow >C{:}CH\cdot CHO$$

dehydrated to an αβ-unsaturated aldehyde; the adduct may be dehydrated before hydrolysis and the resulting βγ-unsaturated aldehyde rearranged to the αβ-isomer. Unlike

$$>CH\cdot \overset{\gamma}{C}(OH)\cdot CH{:}CH\cdot SAc \longrightarrow >C{:}\overset{\gamma}{C}\cdot CH{:}CH\cdot SAc \longrightarrow >C{:}\overset{\gamma}{C}\cdot CH_2\cdot CHO \longrightarrow >CH\cdot \overset{\gamma}{C}{:}CH\cdot CHO$$

the previous attempts, the present method is applicable to primary and secondary, as well as to the tertiary, alcohols.

Since thiolacetic acid and hex-1-yn-3-ol at first gave small yields of adduct, the effects of various factors were studied in detail (>30 experiments). Occasionally experiments under apparently identical conditions gave different results, but some broad generalisations may be made. In all these experiments the yield of the monoadduct was of primary interest, so equimolecular proportions of the reactants were used; in every case practically all the carbinol not converted into adducts was recovered. In general, a low temperature (0°) during the addition favoured formation of the monoadduct. Rapid addition, allowing the thermal effect, favoured formation of the diadduct. Irradiation by ultraviolet light during the addition increased the yield of the monoadducts (from 32·5 to 51%) at low temperature, or of the diadduct (from 14·5 to 22·5%) at the reflux temperature. Addition of as little as 1 mole % of ascaridole increased the yield of the monoadduct (from 34 to 64%) at room temperature; but benzoyl peroxide had no effect

though it catalysed the addition of thiolacetic acid to phenylacetylene (Bader *et al.*, *loc. cit.*) [Cunneen (*J.*, **1947**, **36**, **134**), while this work was in progress, reported similar difference in the action of the two peroxides in the addition of thiolacetic acid to olefins].

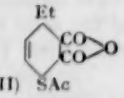
The two products from hex-1-yn-3-ol were identified as 3-hydroxyhex-1-enyl thiolacetate (III) and 1 : 2-diacetylthiohexan-3-ol (IV). Fission of the former adduct with semicarbazide acetate gave the semicarbazone of 3-hydroxyhexanal (V) rather than the derivative of the αβ-unsaturated aldehyde.

$C_3H_7{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}SAc$ (III) $C_3H_7{\cdot}CH(OH){\cdot}CH(SAc){\cdot}CH_2{\cdot}SAc$ (IV) $C_3H_7{\cdot}CH(OH){\cdot}CH_2{\cdot}CHO$ (V)

In attempts to dehydrate the thiolacetate (III), it was recovered unchanged after pyrolysis at 350°, potassium hydrogen sulphate at 100° caused no dehydration, and oxalic acid gave only 6—10% of an impure product. Finally, shaking the ester in benzene with phosphoric oxide at room temperature gave a mixture which on fractionation yielded *ca.* 30% of hexa-1 : 3-dienyl thiolacetate (VII) exhibiting the expected light absorption with a maximum at 2690 Å, together with recovered carbinol and a polymer. The dienyl thiolacetate (VII) was characterised by a maleic anhydride adduct which showed maximal ultraviolet absorption at 2280 Å, in agreement with the structure (VIII).

$C_3H_5{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}SAc \longrightarrow C_3H_5{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CHO \longrightarrow C_3H_7{\cdot}CH{:}CH{\cdot}CHO$

(VII) (VI)



(VIII)

When the dienyl thiolacetate (VII) was treated with cold aqueous-ethanolic semicarbazide acetate, an immediate crystalline precipitate slowly redissolved. Separation of the solid afforded 20% of the semicarbazone of hex-2-enal (VI); redissolution of this semicarbazone in its mother-liquor agrees with an observation by Delaby [*Ann. Chim.* (*France*), 1923, **20**, 211] that the semicarbazones of crotonaldehyde and pent-2-enal redissolve in their mother-liquors owing to ring closure to ketotriazines.

With 1-phenylprop-2-yn-1-ol there were greater difficulties in preparation of the adducts : fission of the monoadduct occurred very readily and was accompanied by dehydration. The yields of monoadduct never exceeded 25%, and of diadduct 18%. Furthermore, separation of products was tedious owing to their high and similar boiling points. Although 3-hydroxy-3-phenylprop-1-enyl thiolacetate (IX) was obtained

(IX) $Ph{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}SAc$ $Ph{\cdot}CH(OH){\cdot}CH(SAc){\cdot}CH_2{\cdot}SAc$ (X)

pure, the diadduct (X) was not, though its light absorption properties leave no doubt as to its constitution. The effect of the conditions of addition was not the same as for hex-1-yn-3-ol : *e.g.*, addition at a higher temperature increased the yield of the monoadduct, irradiation in the cold favoured the formation of both the di- and the mono-adduct, and addition of ascaridole in the cold increased the yield of the diadduct.

Treatment of the monothiolacetate (IX) with a solution of semicarbazide acetate at room temperature gave instantaneously a precipitate of cinnamaldehyde semicarbazone by fission and simultaneous dehydration. The low yield (40%) of the semicarbazone was undoubtedly due to presence of a small amount of impurities in the thiolacetate employed, since in general the yields of the isolated derivatives were markedly decreased by even slight impurities in the thiolacetates.

For a study of tertiary α-ethynylcarbinols (cf. Rupe and Dimroth, *locc. cit.*), ethynyl-*cyclo*hexanol was chosen. Addition of thiolacetic acid in the presence of ascaridole gave a 55—60% yield of crude product, which on slow distillation was dehydrated to a mixture of isomers of 2-*cyclo*hex-1′-enylvinyl thiolacetate (XII), from which one form was isolated

as a solid, m. p. 35·5—36·5°, exhibiting the expected light absorption. Attempts to isolate the alcohol (XI) failed, but 4% of the impure diadduct was obtained; this was formulated as (XIII) on the basis of its ultraviolet absorption (see Table).

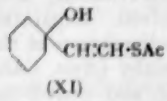
	$\lambda_{max.}$ (Å)	ε		$\lambda_{max.}$ (Å)	ε
C_5H_7·CH(OH)·CH:CH·SAc	2510	8000	C_5H_7·CH(OH)·CH(SAc)·CH_2·SAc	2280	7500
C_6H_9·CH(OH)·CH:CH·SAc ...	2500	6000	C_6H_9·CH(OH)·CH(SAc)·CH_2·SAc	2400	11,500
CH_3·CH(OH)·CH_2·CH:CH·SAc	2280	4000	HO·C_6H_{10}·CH(SAc)·CH_2·SAc	2300	8500
	2520 } 2560 }	7000		2380 *	8000
			CH_3·CH:CH·CH(OH)·CH(SAc)·CH_2·SAc	2330	7500
CH_3·CH(OAc)·CH_2·CH:CH·SAc	2510	7000		2420 *	6500
C_5H_5·CH:CH·CH:CH·SAc	2690	14,500	CH_3·CH(SAc)·CH_2·CH(OH)·C:CH	2300	3500
C_6H_9·CH:CH·SAc, m. p. 35·5—36·5°	2700	10,500	Adduct (VIII)	2370 *	3500
	2780	10,000	Adduct (XIV)	2280	5000
C_6H_9·CH:CH·SAc, liquid	2690	10,500		2330	7000

* Inflexion.

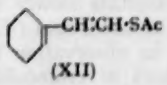
For other compounds containing the chromophores SAc and CH:CH·SAc see Bader, Cross, Heilbron, and Jones (*loc. cit.*).

The dienyl thiolacetate (XII) was also prepared in good yield by dehydration of the crude addition product with anhydrous oxalic acid at 90°, again as a mixture. The ratio of the solid and the liquid product varied but the light absorptions of the two were so similar (see Table) that the oil must be a mixture of geometrical isomers.

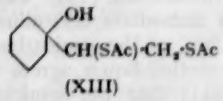
The solid thiolacetate was characterised by a maleic anhydride adduct (XIV) exhibiting an absorption maximum at 2330 Å.



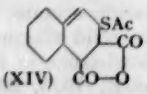
(XI)



(XII)



(XIII)



(XIV)

By the action of semicarbazide on the monothiolacetate (XII) a derivative, m. p. 167°, was obtained in 78% yield. Its absorption maxima indicated that it was a constant-melting 2 : 3 mixture of the semicarbazones of *cyclo*hexylideneacetaldehyde and *cyclo*hexenylacetaldehyde.

Thiolacetic acid added readily to pent-4-yn-2-ol and gave only 4-hydroxypent-1-enyl thiolacetate (XV; R = H), formed in 44% yield when the reaction was carried out under controlled conditions at 0° and in absence of catalysts. Even under vigorous conditions only the monoadduct was formed, its yield being thus raised to 60%. The thiolacetate (XV; R = H) reacted easily with semicarbazide acetate, but the expected semicarbazone

(XV) CH_3·CH(OR)·CH_2·CH:CH·SAc ⟶ CH_3·CH(OR)·CH_2·CH_2·CHO (XVI)

of 4-hydroxypentanal (XVI; R = H) could not be isolated, as its solubility was very similar to that of the by-product, β-acetylsemicarbazide, a difficulty experienced to some degree with all the hydroxysemicarbazones. However, the diacetate (XV; R = Ac) gave the semicarbazone of 4-acetoxypentan-1-al (XVI; R = Ac) on treatment with semicarbazide acetate.

The complexity of the addition of thiols to vinylacetylenes was referred to above. However, it was of interest to effect the reaction with hex-4-en-1-yn-3-ol (XVII), in which the double and the triple bond are not conjugated and thus to compare directly the reactivities of the two groups. The addition occurred in comparatively small yields and under all conditions tried only two of the possible products were obtained, which on the basis of analysis were shown to be a mono- and a di-adduct. The monoadduct showed light absorption (see Table) characteristic of unconjugated thiolacetates (for a discussion of the absorption of thiolacetates see Bader *et al.*, *loc. cit.*) and did not evolve hydrogen sulphide on treatment with ethanolic semicarbazide acetate (which can be considered as a test for vinyl thiolacetates) and so is formulated as (XVIII), formed by addition of thiolacetic acid to the double bond. The suggested orientation of the addition is based on the general observation that, in additions to unsymmetrical unsaturated systems, radicals

attack preferentially at points of high differential electron density with respect to the unsubstituted ethylene (cf. Barton, *Nature*, 1948, **162**, 182). In the alcohol (XVII) $C_{(5)}$ has a higher differential electron density than $C_{(4)}$ and would be expected to be attacked by the thiol radical.

(XVII) $CH_3 \rightarrow \overset{+}{C}H{=}\overset{-}{C}H{\cdot}CH(OH){\cdot}C{\equiv}CH$ $\qquad$ $CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH(OH){\cdot}C{\equiv}CH$ (XVIII)

$CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH(SAc){\cdot}CH_2{\cdot}SAc$ (XIX)

The absorption of the diadduct (see Table), corresponding to two saturated thiolacetate groups, is compatible only with the structure (XIX).

Experimental

Light absorptions were determined for EtOH solutions.

Addition of Thiolacetic Acid to Hex-1-yn-3-ol.—(*a*) To the alcohol (9·8 g., 0·1 mol.; Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 45), cooled in ice and salt, thiolacetic acid (7·6 g., 0·1 mol.) was added dropwise during 50 min. with shaking. The mixture was heated for 1 hr. on the steam-bath, unchanged thiolacetic acid removed under reduced pressure, and the residue fractionated, yielding (i) recovered hex-1-yn-3-ol (4·7 g. 48%), b. p. 45°/13 mm., (ii) *3-hydroxyhex-1-enyl thiolacetate* (6·0 g., 34·5%), a slightly yellowish oil of unpleasant odour, b. p. 76°/5 × 10^{-4} mm., n_D^{16} 1·5050 (Found: S, 18·45. $C_8H_{14}O_2S$ requires S, 18·4%) (light absorption: see Table) (even in great dilution inhalation of the vapours caused violent headaches), and (iii) 1 : 2-*diacetylthiohexan-3-ol* (1·0 g., 4%) as a viscous yellowish oil of unpleasant odour, b. p. 80°/10^{-3} mm., n_D^{20} 1·5208 (Found: S, 25·65. $C_{10}H_{18}O_3S_2$ requires S, 25·6%) (light absorption: see Table).

(*b*) When thiolacetic acid (15·2 g., 0·2 mol.) was added rapidly to hex-1-yn-3-ol (19·6 g., 0·2 mol.) a vigorous reaction ensued. After this has subsided, refluxing was continued for 2 hr. Distillation of the product gave recovered hexynol (7·3 g., 37%), the monothiolacetate (8·0 g., 23%), and the di(thiolacetate) (7·2 g., 14·5%).

(*c*) To hex-1-yn-3-ol (4·9 g., 0·05 mol.) and ascaridole (0·05 g., 0·00025 mol.), cooled in ice, a mixture of thiolacetic acid (3·8 g., 0·05 mol.) and ascaridole (0·05 g.) was added during 10 min. After 26 hr. at room temperature distillation yielded the recovered acetylene (1·5 g., 31%) and the monothiolacetate (5·85 g., 67%).

(*d*) A solution of thiolacetic acid (3·8 g.) in ether (30 c.c.) was added dropwise during 20 min. to hex-1-yn-3-ol (4·9 g.) contained in a silica tube provided with an internal glass spiral through which cold water was circulated, and exposed at about 15 cm. to a mercury-vapour lamp during the addition and for a further 3 hr. The ether was removed and distillation gave recovered hexynol (1·95 g., 40%) and the monothiolacetate (4·45 g., 51%).

(*e*) As in (*d*) but without ether. After the addition, the mixture was refluxed for 7½ hr. during further irradiation. Distillation gave recovered hexynol (0·5 g., 10%), the monoadduct (0·5 g., 6%), and the diadduct (2·8 g., 22·5%).

Conversion of 3-Hydroxyhex-1-enyl Thiolacetate (III) *into the Semicarbazone of 3-Hydroxyhexanal* (V).—To a solution of semicarbazide acetate (from the hydrochloride, 1·2 g., in 80% alcohol, 6·5 c.c.), 3-hydroxyhex-1-enyl thiolacetate (0·87 g.) was added and the mixture was warmed to 50° and set aside at room temperature for 30 hr. The yellow oil obtained by evaporation under reduced pressure crystallised in contact with ether (2 c.c.). It was extracted with hot chloroform, and the residue on crystallisation from alcohol gave *3-hydroxyhexanal semicarbazone* (0·5 g., 60%), prisms, decomp. 149° (Found: N, 24·55. $C_7H_{15}O_2N_3$ requires N, 24·25%), having no intense light absorption above 2150 Å.

Hexa-1 : 3-dienyl Thiolacetate (VII).—Phosphoric oxide (3·5 g.) was added to a solution of 3-hydroxyhex-1-enyl thiolacetate (2·9 g.) in dry benzene (40 c.c.). After 19 hours' shaking in nitrogen at 20° the mixture was treated with water. The aqueous layer was extracted with benzene, and the combined benzene extracts were washed with sodium hydrogen carbonate solution and dried. Fractionation of the residue obtained on evaporation yielded slightly impure hexa-1 : 3-dienyl thiolacetate (0·73 g., 30%), b. p. 66°/10^{-3} mm., $n_D^{20\cdot5}$ 1·5330, having a faintly unpleasant odour (Found: S, 19·25. Calc. for $C_8H_{12}OS$: S, 20·5%) (light absorption: see Table), recovered alcohol (0·55 g., 19%), b. p. 78°/10^{-3} mm., and a liquid (0·60 g., 23%), b. p. 102—109°/10^{-3} mm., $n_D^{20\cdot5}$ 1·5228.

The diene thiolacetate (0·31 g.) and maleic anhydride (0·20 g.) were refluxed in benzene (0·5 c.c.) for 15 min. After 3 days at 0° the *adduct* (VIII) (0·06 g.), m. p. 108—109·5°, separated

as prisms. It crystallised from aqueous ethanol in plates, m. p. 113° (Found: S, 12·6. $C_{12}H_{14}O_4S$ requires S, 12·6%) (light absorption: see Table).

Conversion of Hexa-1:3-dienyl Thiolacetate (VII) *into Hex-2-enal Semicarbazone.*—The thiolacetate (0·78 g.) was added to a solution of semicarbazide acetate (from the hydrochloride, 1·2 g.) in 90% ethanol (13 c.c.), causing a precipitation of fine crystals. After 20 min. at room temperature the solid was separated, then dried *in vacuo*. Hex-2-enal semicarbazone (0·155 g., 20%), m. p. 172—174°, crystallised from 1:1 aqueous ethanol (1 c.c.) in needles, m. p. 174° [Kroper and Pinkernelle, *Ber.*, 1934, **67**, 269, give m. p. 173°; Delaby and Guillot, *Bull. Soc. chim.* (*France*), 1933, **53**, 30, give m. p. 175—176°].

Addition of Thiolacetic Acid to 1-Phenylprop-2-yn-1-ol.—(*a*) Thiolacetic acid (7·6 g., 0·1 mol.) in ether (20 c.c.) was added during 15 min. to the propynol (13·2 g., 0·1 mol.; Jones and McCombie, *J.*, 1942, 733) contained in an internally cooled silica tube, exposed to ultraviolet irradiation during the addition and for a further 3 hr. Then the mixture was set aside for 7 days at 20°. Fractionation of the residue gave: (i) recovered phenylpropynol (4·95 g., 37·5%), b. p. 74—76°/10^{-3} mm.; (ii) *3-hydroxy-3-phenylprop-1-enyl thiolacetate* (4·95 g., 23·8%), a yellow, viscous oil with a sweet, nauseating odour, b. p. 120—122°/10^{-3} mm., $n_D^{20\cdot5}$ 1·5670—1·5750, which after two redistillations had b. p. 115°/10^{-3} mm., n_D^{20} 1·5730 (Found: S, 15·35. $C_{11}H_{12}O_2S$ requires S, 15·4%); and (iii) *1:2-diacetylthio-3-phenylpropan-3-ol* (3·05 g., 10·7%) as a reddish, viscous oil with nauseating odour, b. p. 123—128°/10^{-3} mm., n_D^{20} 1·5857—1·5904 (Found: S, 21·0. $C_{13}H_{16}O_3S_2$ requires S, 22·5%). Light absorption data for both compounds are given in the Table.

(*b*) The following yields were obtained under other conditions:

	Monoadduct (%)	Diadduct (%)
Slow addition at 0°, then reflux	3	5
Rapid addition, then reflux	17	0
With 1% of ascaridole	6	18

Conversion of 3-Hydroxy-3-phenylprop-1-enyl Thiolacetate (IX) *into Cinnamaldehyde Semicarbazone.*—The thiolacetate (1·04 g.) was added to a solution of semicarbazide acetate (from the hydrochloride, 1·2 g.) in 85% ethanol (7 c.c.). Hydrogen sulphide was at once evolved at room temperature and a crystalline precipitate formed. After 1 day at 20° the semicarbazone (0·39 g., 40%) was isolated as plates, which after recrystallisation from ethanol melted at 207°, undepressed on admixture with cinnamaldehyde semicarbazone (m. p. 208°).

Addition of Thiolacetic Acid to 1-Ethynylcyclohexanol.—A mixture of thiolacetic acid (7·6 g., 0·1 mol.) and ascaridole (0·1 g.) was added dropwise during 30 min. with stirring to 1-ethynylcyclohexanol (12·4 g., 0·1 mol.) and ascaridole (0·1 g.), cooled in ice. After 2 days at 20° the mixture was neutralised with a saturated solution of sodium hydrogen carbonate and extracted several times with ether. Isolation in the usual manner and distillation gave recovered ethynylcyclohexanol (3·7 g., 30%), b. p. 69—72°/15 mm., (ii) a colourless liquid with a pleasant odour, b. p. 95—122°/10^{-4} mm., n_D^{22} 1·5328—1·5390 (a mixture of a monoadduct and its dehydration product) (10·3 g., *ca.* 57%), and impure 1-(1:2-diacetylthioethyl)cyclohexanol (XIII) (1·1 g., 4%), a colourless liquid with a pleasant odour, b. p. 95°/5 × 10^{-3} mm., n_D^{18} 1·5460 (Found: S, 21·6. $C_{12}H_{20}O_3S_2$ requires S, 23·6%). This product was not obtained pure even after repeated distillation. For light absorption, see Table.

Dehydration. (*a*) The crude monoadduct (16·15 g.) was heated at 95° for 2 hr. at 15 mm. in presence of anhydrous oxalic acid (16·0 g.) activated by entrainment distillation with carbon tetrachloride immediately before use. Water was added and the product isolated by use of light petroleum (b. p. 40—60°). Removal of the solvent and distillation gave an oil, b. p. 85—89°/5 × 10^{-3} mm., n_D^{17} 1·5700 (8·6 g., 55%), which solidified almost completely. Recrystallisation from light petroleum (b. p. 40—60°) at −30° gave 2-cyclohex-1′-enylvinyl thiolacetate (5·55 g.) as colourless prismatic needles, m. p. 35·5—36·5°, which very readily darkened and liquefied in air and light (Found: S, 17·45. $C_{10}H_{14}OS$ requires S, 17·6%). Absorption max. at 2700 and 2780 Å (ε 10,500 and 10,000 respectively). After removal of the solid, the residual oil distilled at 85°/0·05 mm. (n_D^{19} 1·5575), but did not yield any more solid: its absorption max. was at 2690 Å (ε 10,400). The overall yield of the isomeric mixture, based on ethynylcyclohexanol, was 31%.

(*b*) The crude monoadduct (3·95 g.) was twice slowly redistilled through a 10-cm. Vigreux column. A homogeneous liquid was obtained, having b. p. 79°/10^{-3} mm., n_D^{22} 1·5729 (3·75 g., 95%), which in ice and salt solidified partly, giving a mixture of isomers as in (*a*).

The solid diene thiolacetate (0·91 g.) and maleic anhydride (0·49 g.) were refluxed for 15 min.

in benzene (0·5 c.c.). After 24 hr. at 0° a brown solid was deposited. It was extracted with hot *cyclo*hexane and the extract decolorised over charcoal and kept at 0° for 12 hr. *3-Acetylthio-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydronaphthalene-1 : 2-dicarboxylic anhydride* (XIV) (0·445 g., 32%) separated as needles, m. p. 103—103·5° (Found : C, 60·0; H, 5·75; S, 11·2. $C_{14}H_{16}O_4S$ requires C, 60·0; H, 5·75; S, 11·45%) (light absorption, see Table).

Conversion of 2-cyclo*Hex-1'-enylvinyl Thiolacetate* (XII) *into* cyclo*Hexenylacetaldehyde and* cyclo*Hexylideneacetaldehyde Semicarbazones.*—The thiolacetate (0·91 g.) was heated under reflux for 2½ hr. with ethanolic semicarbazide acetate (from the hydrochloride, 1·2 g.). By slow addition of water with simultaneous trituration a solid mixture was precipitated (0·71 g., 78%; m. p. 157—158°). Recrystallisation from water gave the mixed semicarbazones as needles, m. p. 167° (Found : C, 60·1; H, 8·7; N, 22·85. Calc. for $C_9H_{15}ON_3$: C, 59·7; H, 8·3; N, 23·2%). The absorption max. were at 2290 and 2720 Å (ε 10,900 and 11,300 respectively), indicating about 60% of *cyclo*hexenylacetaldehyde and 40% of *cyclo*hexylideneacetaldehyde semicarbazones [Aldersley and Burkhardt (*loc. cit.*) reported maximum at 2720 Å (ε 28,000); Dimroth (*loc. cit.*) gave 2740 Å (ε 32,300); Chanley (*loc. cit.*) gave 2690 Å (ε 33,800)].

Addition of Thiolacetic Acid to Pent-4-yn-2-ol.—(*a*) When thiolacetic acid (15·2 g., 0·2 mol.) was quickly added to a mixture of pent-4-yn-2-ol (16·6 g., 0·2 mol.) (Haynes and Jones, *J.*, 1946, 956) and ascaridole (0·34 g., 0·002 mol.) an extremely violent reaction ensued after an induction period (3—5 min.). After the mixture had boiled, the refluxing was continued for another 3 hr. The unchanged thiolacetic acid was then removed under reduced pressure and the residue fractionated, yielding recovered pentynol (5·8 g., 35%), b. p. 52°/27 mm., and *4-hydroxypent-1-enyl thiolacetate* (19·0 g., 60%), a colourless liquid with a faint sweet odour, b. p. 76°/5 × 10^{-4} mm., $n_D^{22.5}$ 1·5158 (Found : S, 19·75. $C_7H_{12}O_2S$ requires S, 20·0%) (light absorption, see Table).

(*b*) Under the same conditions but in absence of ascaridole a yield of 44% of the monoadduct was obtained with recovery of 39% of the acetylene.

4-Acetoxypent-1-enyl Thiolacetate (XV; R = Ac).—To a mixture of 4-hydroxypent-1-enyl thiolacetate (15·9 g.) and pyridine (9·2 c.c.), cooled in ice and salt, acetic anhydride (9·5 c.c.) was added and the mixture kept at 20° for 60 hr. Water (100 c.c.) and ether (100 c.c.) were then added, and the product isolated in the usual manner. Distillation gave *4-acetoxypent-1-enyl thiolacetate* (18·7 g., 93%), a colourless liquid with a sweet fruity smell, b. p. 83°/0·05 mm., $n_D^{19.5}$ 1·4910 (Found : C, 53·55; H, 7·35; S, 16·3. $C_9H_{14}O_3S$ requires C, 53·45; H, 7·0; S, 15·9%) (light absorption, see Table).

Conversion of 4-Acetoxypent-1-enyl Thiolacetate into 4-Acetoxypentan-1-al Semicarbazone (cf. XVI; R = Ac).—The diacetate (1·0 g., 0·005 mol.) was refluxed for 13 hr. with semicarbazide acetate (from the hydrochloride, 1·2 g., 0·011 mol.) in 90% ethanol (13 c.c.). Evaporation under reduced pressure left a gum which solidified on prolonged trituration with ether and was then extracted with hot benzene. To the partly evaporated extract light petroleum (b. p. 40—60°) was added until precipitation commenced. At 0° the *semicarbazone* (0·28 g., 28%) separated in prisms, m. p. 86·5° (Found : C, 47·9; H, 7·65; N, 20·6. $C_8H_{15}O_3N_3$ requires C, 47·75; H, 7·5; N, 20·9%).

Addition of Thiolacetic Acid to Hex-4-en-1-yn-3-ol.—The alcohol (9·6 g., 0·1 mol.) (Heilbron, Jones, and Weedon, *J.*, 1945, 81) was treated with thiolacetic acid (7·6 g., 0·1 mol.), added during 20—30 min. at 0° (see Table below), and the resultant solution was kept for 24 hr. at 20°. Fractionation of the product gave recovered hexenynol, b. p. 60—61°/15 mm., *3-hydroxy-1-methylpent-4-ynyl thiolacetate* (XVIII), b. p. 67°/10^{-4} mm., $n_D^{26.5}$ 1·5007 (Found : S, 18·8. $C_8H_{12}O_2S$ requires S, 18·6%), and 1 : *2-diacetylthiohex-4-en-3-ol* (XIX), a mobile liquid with a nauseating odour, b. p. 100°/10^{-4} mm., $n_D^{23.5}$ 1·5407 (Found : S, 25·45. $C_{10}H_{16}O_3S_2$ requires S, 25·8%). Light absorption data for both compounds are given in the Table. The yields obtained under varied conditions are :

	Monoadduct (%)	Diadduct (%)
No catalyst	6	6
With 1% of ascaridole	25	11
No catalyst; ultraviolet irradiation	12	13·5

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24. *Polynuclear Heterocyclic Systems. Part IX.*† n-π^*-*Transitions in the Spectra of Aromatic Aza-hydrocarbons.*

By G. M. Badger and I. S. Walker.

The ultraviolet spectra of a number of polycyclic aromatic aza-hydrocarbons have been examined in both ethanol (polar solvent) and *cyclo*hexane or carbon tetrachloride (non-polar solvents). Three main regions of absorption, similar to those given by the corresponding aromatic hydrocarbons, are generally obtained. In the long-wavelength region many of the aza-compounds show an additional absorption region (particularly in non-polar solvents) which has been assigned to a transition involving the promotion of a non-bonding electron from the nitrogen atom to an unfilled π orbital (n–π^* transition).

When ethanol is used as a solvent, the ultraviolet and visible absorption spectra of the aromatic aza-hydrocarbons (pyridine, quinoline, phenanthridine, etc.) resemble those of the corresponding aromatic hydrocarbons very closely (Badger, Pearce, and Pettit, *J.*, 1951, 3199). Three main regions of absorption (designated the group I, II, and III bands) can usually be distinguished in both carbocyclic and heterocyclic series. These absorption bands correspond to π–π^* electronic transitions and move progressively to longer wavelengths as the number of rings increases. In addition, and especially in *cyclo*hexane and other non-polar solvents, a number of monocyclic aromatic aza-hydrocarbons have been shown to give a further absorption band at longer wavelengths than the group-III absorption. These long-wavelength bands have been assigned to transitions involving the excitation of an electron from a non-bonding orbital on the nitrogen atom (n-electron) to an unoccupied π orbital (n–π^* transition) (Halverson and Hirt, *J. Chem. Phys.*, 1951, **19**, 711; Hirt and Schmidt, *ibid.*, 1955, **23**, 600; Platt, *J. Opt. Soc. Amer.*, 1953, **43**, 252; Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14; McConnell, *J. Chem. Phys.*, 1952, **20**, 700).

In polar solvents (ethanol, water, etc.) the solvent–solute interactions, probably involving hydrogen bonding in most cases, change the character of the non-bonding orbital, and the absorption resulting from n–π^* transitions is shifted to shorter wavelengths, where it is often more or less hidden under the group-III (π–π^*) absorption bands. Polar solvents also appear to smooth out much of the fine structure. It seemed likely that the relatively intense long-wavelength absorption obtained with the polycyclic aromatic aza-hydrocarbons in ethanol (Badger, Pearce, and Pettit, *loc. cit.*) might be due to a superposition of the group-III and n–π^* absorptions. A number of such compounds have accordingly been examined not only in ethanol (as a polar solvent), but also in *cyclo*hexane or in carbon tetrachloride (as non-polar solvents) in an attempt to resolve the two band systems.

In *cyclo*hexane solution the n–π^* transition of pyridine appears as a series of shoulders on the long-wavelength side of the group-III bands; but with monocyclic diazines, it becomes a well-defined band at long wavelengths. Pyridazine, for example, gives a distinct n–π^* absorption band (in *cyclo*hexane) with a maximum around 3450 Å, the group-III absorption (π–π^*) having a maximum around 2500 Å, similar to that of benzene. In water as a polar solvent the n–π^* band was found to be shifted to shorter wavelengths, the maximum being about 3000 Å (Halverson and Hirt, *loc. cit.*; Evans and Wiselogle, *J. Amer. Chem. Soc.*, 1945, **67**, 60).

The spectra of the dicyclic diazines also show well-defined n–π^* absorption bands. With cinnoline (I) in *cyclo*hexane (Hearne, Morton, and Simpson, *J.*, 1951, 3318) the absorption below 2300 Å clearly corresponds to the group-I bands in naphthalene, the two maxima at 2755 and 2860 Å correspond to the group-II bands, the three maxima at 3085, 3170, and 3225 Å to the group-III region; and the low-intensity absorption with a maximum at 3900 Å may be identified as an n–π^* transition. With quinoxaline (II) in ethanol the group-III bands are far more intense than the corresponding bands in naphthalene and

† Part VIII, *J.*, 1954, 2329.

there is a pronounced shoulder at long wavelengths due to the superposition of the n–π^* absorption. In *cyclo*hexane this n–π^* absorption moves to longer wavelengths and has some fine structure (Fig. 1).

The absorption spectrum of phthalazine (III) is somewhat similar (Hirt, personal

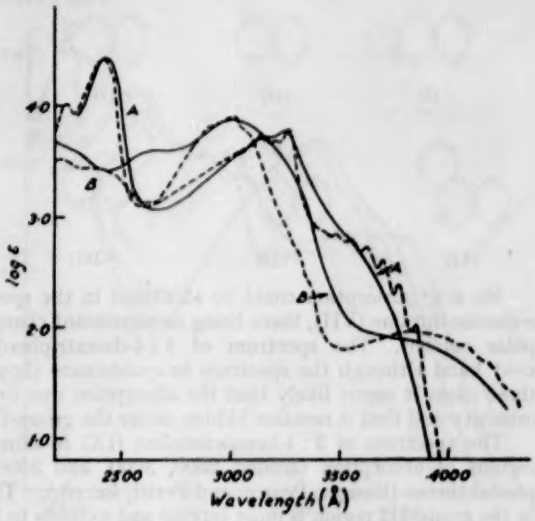


FIG. 1. *Absorption curves of (A) quinoxaline and (B) pteridine in ethanol* (——) *and* cyclo*hexane* (– – – –).

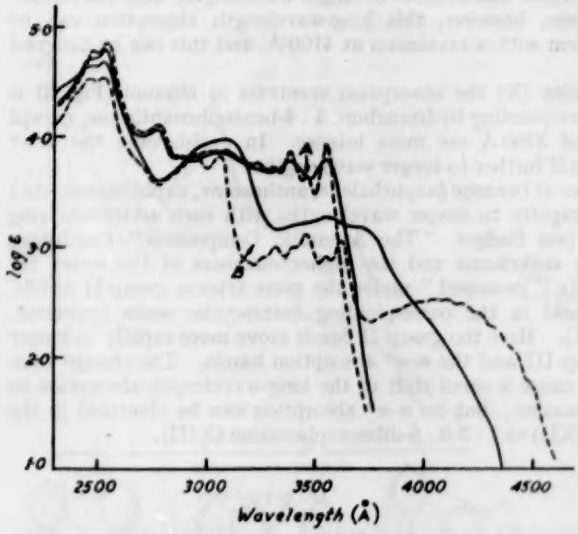


FIG. 2. *Absorption curves of (A) 1 : 4-diazatriphenylene and (B) 3 : 4-benzocinnoline in ethanol* (——) *and* cyclo*hexane* (– – – –).

communication), the n–π^* absorption appearing as a shoulder in ethanol solution, and as a more pronounced shoulder at longer wavelengths in *cyclo*hexane. The spectrum of 1 : 4-diphenylphthalazine (IV) has now been examined in ethanol, in *cyclo*hexane, and in carbon tetrachloride. Here again the n–π^* absorption appears as a shoulder in ethanol and moves to longer wavelengths in the non-polar solvents. In this and in some other cases, carbon tetrachloride and *cyclo*hexane were found to be interchangeable, the same absorption curve being obtained in both solvents.

The spectra of pteridine (V) in polar and non-polar solvents may be compared with those of quinoxaline. The absorption around 3000 Å corresponds to the group-III absorption and the n–π^* absorption appears as a shoulder in ethanol and as a distinct band (at somewhat longer wavelength) in *cyclo*hexane (Fig. 1).

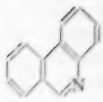
(I)

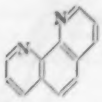
(II)

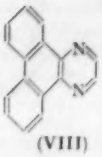
(III)

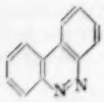
(IV)

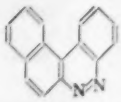
(V)


(VI)


(VII)


(VIII)


(IX)

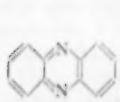

(X)

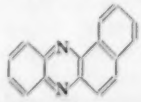
No n–π^* absorption could be identified in the spectra of phenanthridine (VI) and of *o*-phenanthroline (VII), there being no significant change in moving from a polar to a non-polar solvent. The spectrum of 1 : 4-diazatriphenylene (VIII) likewise showed no n–π^* band although the spectrum in *cyclo*hexane shows more fine structure (Fig. 2). In these cases it seems likely that the absorption due to the n–π^* transition is of very low intensity and that it remains hidden under the group-III (π–π^*) bands.

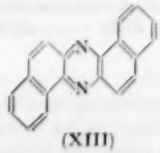
The spectrum of 3 : 4-benzocinnoline (IX) in ethanol (Fig. 2) shows the three main regions of absorption (around 2500, 3000, and 3500 Å) analogous to those given by phenanthrene (Badger, Pearce, and Pettit, *loc. cit.*). The chief difference is that absorption in the group-III region is more intense and extends to longer wavelengths with the heterocyclic compound. In *cyclo*hexane, however, this long-wavelength absorption can be resolved as a separate band system with a maximum at 4100 Å, and this can be assigned to the n–π^* transition.

With 3 : 4-5 : 6-dibenzocinnoline (X) the absorption spectrum in ethanol (Fig. 3) is again similar to that of the corresponding hydrocarbon, 3 : 4-benzophenanthrene, except that the group-III bands around 3700 Å are more intense. In *cyclo*hexane the n–π^* transition shifts the absorption still further to longer wavelengths.

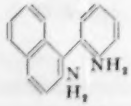
In a series of linear benzologues of benzene (naphthalene, anthracene, naphthacene, etc.) the group-II bands move more rapidly to longer wavelengths with each additional ring than do the group-III bands (see Badger, "The Aromatic Compounds," Cambridge Univ. Press, 1954, p. 393). In anthracene and the higher members of the series, for example, the group-III bands are "swamped" under the more intense group-II bands. A similar situation seems to hold in the corresponding heterocyclic series [pyrazine, quinoxaline, phenazine (XI), etc.]. Here the group-II bands move more rapidly to longer wavelengths than both the group-III and the n–π^* absorption bands. The change from polar to non-polar solvent does cause a small shift of the long-wavelength absorption to still longer wavelengths for phenazine; but no n–π^* absorption can be identified in the spectra of 1 : 2-benzophenazine (XII) or 1 : 2-5 : 6-dibenzophenazine (XIII).


(XI)


(XII)


(XIII)

(XIV)



(XV)

On the other hand, although the spectrum of 5 : 6 : 11 : 12-tetra-azanaphthacene (XIV) in a polar solvent (chloroform) is similar to that of the corresponding hydrocarbon in the 2000—5000 Å region, the heterocyclic compound shows increased absorption at long wavelengths, with a "tail" extending to 6000 Å (Fig. 4). In a non-polar solvent (carbon

tetrachloride) this long-wavelength absorption is resolved as an additional absorption region between 5000 and 6400 Å. Here again, therefore, a n–π^* transition seems to be involved.

Most of the compounds required for this investigation were prepared by known methods. 3 : 4-5 : 6-Dibenzocinnoline (X), however, was prepared by the oxidation of 1-*o*-aminophenyl-2-naphthylamine (XV) with Caro's acid.

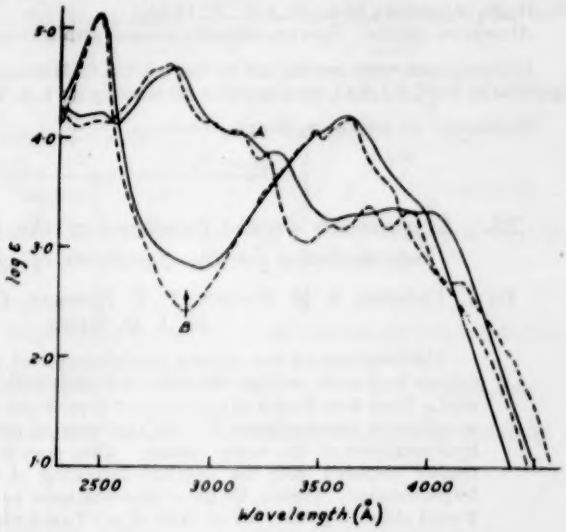


FIG. 3. *Absorption curves of* (*A*) 3 : 4-5 : 6-*dibenzocinnoline and* (*B*) *phenazine in ethanol* (——) *and cyclohexane* (– – – – –).

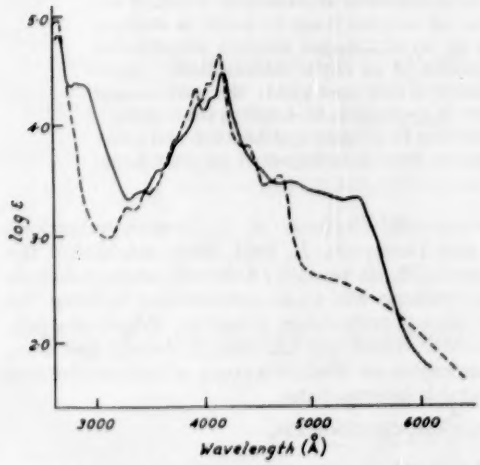


FIG. 4. *Absorption curves of* 5 : 6 : 11 : 12-*tetra-azanaphthacene in chloroform* (——) *and carbon tetrachloride* (– – – – –).

Experimental.—Materials. We are indebted to Professor A. Albert for a generous gift of pteridine, and to Mr. R. G. Buttery for the 1 : 2-5 : 6-dibenzophenazine. Other compounds were prepared as follows: quinoxaline, Cavagnol and Wiselogle, *J. Amer. Chem. Soc.*, **1947**, **69**, 795; 1 : 4-diphenylphthalazine, Guyot and Catel, *Compt. rend.*, 1905, **140**, 1348; 1 : 2-benzophenazine, Ullmann, and Heisler, *Ber.*, **1909**, **42**, 4263; 3 : 4-benzocinnoline, Badger, Seidler, and Thomson, *J.*, 1951, 3207; 1 : 4-diazatriphenylene, Mason, *Ber.*, 1886, **19**, 112; 5 : 6 : 11 : 12-tetra-aza-naphthacene, Hinsberg and Pollak, *Ber.*, 1896, **29**, 784.

3 : 4-5 : 6-*Dibenzocinnoline.* 1-*o*-Aminophenyl-2-naphthylamine (XV) was prepared in 25% yield according to the method of Fucks and Nizel (*Ber.*, 1927, **60**, 209) and had m. p. 154-5°.

Ammonium persulphate (12·4 g.) was added to 92% sulphuric acid (13·2 g.), and the mixture was shaken until all dissolved (1 hr.). The solution was then diluted with ice (55 g.), and finally the diamine (3·0 g.) was added all at once. After 3 min. the solution was poured on ice (200 g.) and basified with sodium carbonate. The precipitate was dried, and purified by chromatography in benzene on alumina. Recrystallisation from benzene–hexane gave 3 : 4-5 : 6-*dibenzocinnoline* (0·5 g.) as yellow leaflets, m. p. 156·5—157·5° (Found: C, 83·4; H, 4·3; N, 12·5. $C_{16}H_{10}N_2$ requires C, 83·5; H, 4·4; N, 12·2%).

Absorption spectra. Spectra were determined with a Hilger Uvispek spectrophotometer.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory. We are also grateful to the C.S.I.R.O. for a research scholarship (to I. S. W.).

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, August 4th*, 1955.]

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25. *Experiments on the Synthesis of the Pyrethrins. Part X.* Intermediates for the Synthesis of cis-Pyrethrolone.†*

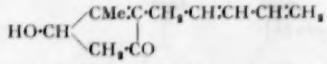
By L. CROMBIE, S. H. HARPER, F. C. NEWMAN, D. THOMPSON, and (in part) R. J. D. SMITH.

The reactions of the toluene-*p*-sulphonates of pent-2-yne-1 : 5-diol with sodium hydroxide, sodium ethoxide, and ethyl sodioacetoacetate are investigated. Pent-4-en-2-yn-1-ol and oct-7-en-5-yn-2-one are obtained in poor yield as potential intermediates for the synthesis of *cis*-pyrethrolone by partial hydrogenation of the enyne system. Pent-4-en-2-yn-1-ol, however, is more readily prepared from the Grignard derivative of vinylacetylene and paraformaldehyde. Thence, by the acetoacetic ester ketone synthesis, pent-4-en-2-ynyl chloride gives a better yield of oct-7-en-5-yn-2-one.

Extension of these reactions to the preparation of *cis*-octa-5 : 7-dien-2-one from toluene-*p*-sulphonyl derivatives of *cis*-pent-2-ene-1 : 5-diol is studied, since construction of the *cis*-system by an elimination reaction would avoid difficulties encountered on hydrogenation of an enyne intermediate. However, *cis*-octa-5 : 7-dien-2-one is obtained in only poor yield; the predominant reaction with ethyl sodioacetoacetate is cyclisation to 4-acetyl*cyclo*hexene.

The possibility of using this cyclisation to prepare *cyclo*heptene and *cyclo*octene analogues of 4-acetyl*cyclo*hexene, from homologues of *cis*-pent-2-ene-1 : 5-diol, is explored.

THE degradative experiments and stereospecific synthesis of (±)-*trans*-pyrethrolone described in Part VII (Crombie, Harper, and Thompson, *J.*, 1951, 2906) established the structure of pyrethrolone as 4-hydroxy-3-methyl-2-(*cis*-penta-2 : 4-dienyl)*cyclo*pent-2-en-1-one (I). Attention is now directed to the synthesis of (±)-*cis*-pyrethrolone utilising the routes previously devised for alkyl- and alkenyl-rethrolones (Crombie, Edgar, Harper, Lowe, and Thompson, *J.*, 1950, 3552; Schechter, Green, and LaForge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165). In this and a later communication we describe a study of the introduction of the *cis*-penta-2 : 4-dienyl system into suitable intermediates.

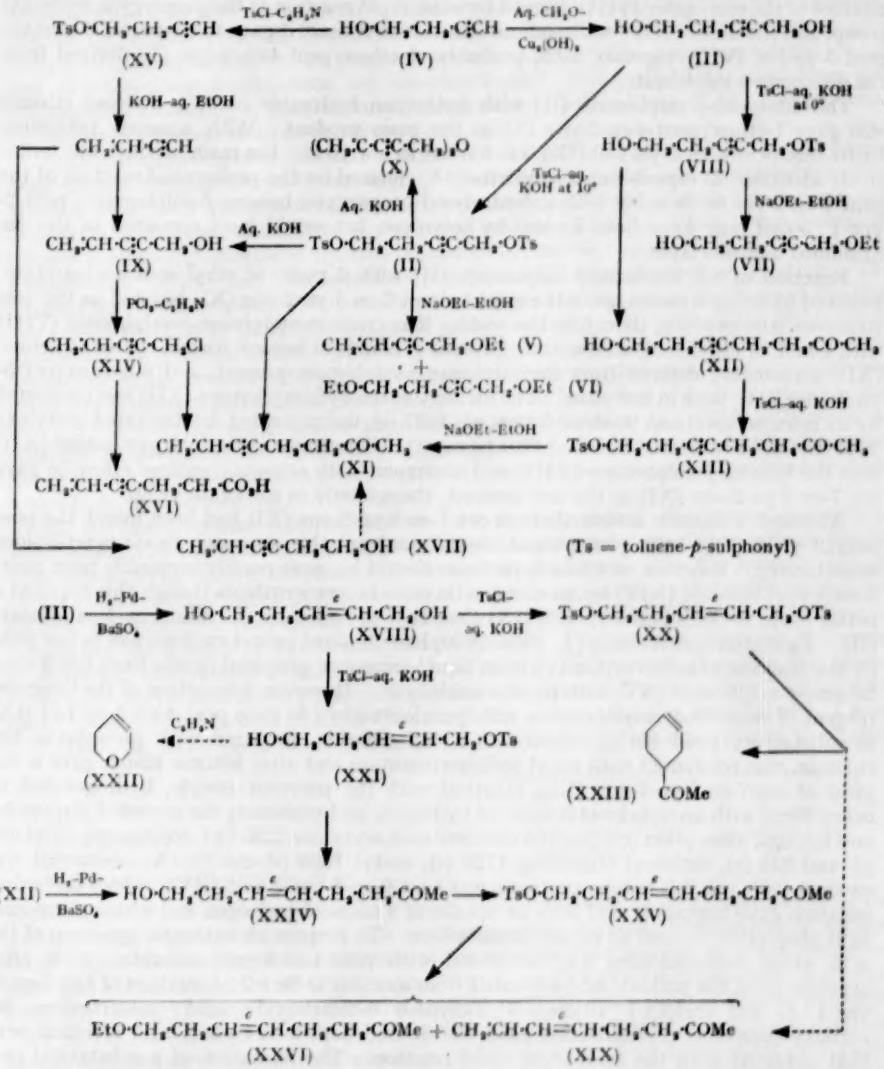
(I) 

The discovery by Eglington and Whiting (*J.*, 1950, 3650; 1953, 3052) that the toluene-*p*-sulphonates of two βγ-acetylenic alcohols, but-3-yn-1-ol and pent-4-yn-2-ol, lose toluene-*p*-sulphonic acid on treatment with strong alkali to form the vinylacetylene in high yield, while with sodiomalonic ester substitution occurs only to the extent of 3%, suggested means by which a ·CH_2·C:C·CH:CH_2 side-chain could be introduced, subsequently to be selectively

* Part IX, *J.*, 1955, 779.

† Read in abstract at the XIVth International Congress of Pure and Applied Chemistry, Zürich, July, 1955.

hydrogenated to the *cis*-penta-2 : 4-diene system. For this purpose the ditoluene-*p*-sulphonate (II) of pent-2-yne-1 : 5-diol (III) appeared particularly suitable for the β-sulphonyloxy-group should undergo elimination and the α-(propargylic)sulphonyloxy-group, owing to its pseudohalogen character, should undergo nucleophilic replacement.



Pent-2-yne-1 : 5-diol (III), prepared by hydroxymethylation of but-3-yn-1-ol (IV) with formaldehyde in the presence of cuprous hydroxide and since described by Heuberger and Owen (*J.*, 1952, 910), was converted in good yield into the crystalline ditoluene-*p*-sulphonate (II). The crude ester with sodium ethoxide in ethanol gave, as main product though in only moderate yield, the expected 1-ethoxypent-4-en-2-yne (V), whose ultraviolet absorption (max. at 229 mμ, ε 9000) was characteristic of the enyne chromophore. A higher-boiling

product appeared from analyses to be a mixture of 1 : 5-diethoxypent-2-yne (VI), derived by double replacement, and 5-ethoxypent-3-yn-1-ol (VII), formed by replacement from the monotoluene-*p*-sulphonate, a likely contaminant in the crude ditoluene-*p*-sulphonate. A liquid monotoluene-*p*-sulphonate was prepared by reaction of pent-2-yne-1 : 5-diol with 1 mol. of toluene-*p*-sulphonyl chloride in aqueous potassium hydroxide, and behaved as a mixture of the monoester (VIII), formed by more rapid reaction at the propargylic hydroxyl group, and the diester (II): with sodium ethoxide in ethanol it gave the expected 5-ethoxypent-3-yn-1-ol (VII), together with, probably, 1-ethoxypent-4-en-2-yne (V) derived from the ditoluene-*p*-sulphonate.

The ditoluene-*p*-sulphonate (II) with potassium hydroxide in 50% aqueous ethanol still gave 1-ethoxypent-4-en-2-yne (V) as the main product. With aqueous potassium hydroxide pent-4-en-2-yn-1-ol (IX) was formed in low yield: the main product was tentatively identified as dipent-4-en-2-ynyl ether (X), formed by the preferential reaction of the pent-4-en-2-yne oxide anion with unhydrolysed propargylic toluene-*p*-sulphonate; pent-2-yne-1 : 5-diol may have been formed by solvolysis but would have remained in the unexamined aqueous layer.

Reaction of the ditoluene-*p*-sulphonate (II) with 2 mols. of ethyl sodioacetoacetate, followed by ketonic fission, gave the expected oct-7-en-5-yn-2-one (XI) isolated as the sole steam-volatile product, though in low yield. The crude monotoluene-*p*-sulphonate (VIII) with 1 mol. of ethyl sodioacetoacetate gave, as products of ketonic fission, the same ketone (XI), presumably derived from the ditoluene-*p*-sulphonate present, and 8-hydroxyoct-5-yn-2-one (XII), both in low yield. The identity of the hydroxy-ketone (XII) was confirmed by its infrared spectrum [hydroxyl 3390 (s), 1037 (s), unconjugated disubstituted acetylene 2247 (w), and α-saturated carbonyl 1704 (s) cm.$^{-1}$]. Conversion of the hydroxy-ketone (XII) into the toluene-*p*-sulphonate (XIII) and treatment with ethanolic sodium ethoxide gave oct-7-en-5-yn-2-one (XI) as the sole product, though only in moderate yield.

Although a suitable intermediate in oct-7-en-5-yn-2-one (XI) had been found, the poor overall yield (7%) from pent-2-yne-1 : 5-diol rendered this approach to *cis*-pyrethrolone unattractive. However, oct-7-en-5-yn-2-one should be more readily accessible from pent-4-en-2-ynyl chloride (XIV) by an acetoacetic ester ketone synthesis though this required a better route to pent-4-en-2-yn-1-ol (IX) than that provided by the ditoluene-*p*-sulphonate (II). Eglington and Whiting (*J.*, 1950, 3650) had obtained pent-4-en-2-yn-1-ol in low yield by the reaction of sodiovinylacetylene in liquid ammonia, prepared *in situ* from but-3-ynyl toluene-*p*-sulphonate (XV) with paraformaldehyde. However, interaction of the Grignard reagent of redistilled vinylacetylene with paraformaldehyde gave pent-4-en-2-yn-1-ol (IX) in satisfactory yield (50%). Pent-4-en-2-ynyl chloride, prepared with phosphorus trichloride, was condensed with ethyl sodioacetoacetate and after ketonic fission gave a fair yield of oct-7-en-5-yn-2-one (XI), identical with the previous sample, hydrogenated to octan-2-one with an uptake of 3 mols. of hydrogen, and posesssing the expected ultraviolet and infrared absorption [conjugated disubstituted acetylene 2231 (w), conjugated vinyl 976 (s) and 921 (s), carbonyl stretching 1720 (s), acetyl 1365 (s) cm.$^{-1}$]. A substantial by-product (20%) in this ketone synthesis was hept-6-en-4-ynoic acid (XVI), which on hydrogenation gave heptanoic acid with an uptake of 3 mols. of hydrogen and whose ultraviolet light absorption showed an enyne chromophore. To prepare an authentic specimen of the acid, ethyl sodiomalonate was condensed with pent-4-en-2-ynyl chloride: even after crystallisation the malonic acid appeared from analysis to be a 2 : 1 mixture of hex-5-en-3-yne-1 : 1- and undeca-1 : 10-diene-3 : 8-diyne-6 : 6-dicarboxylic acid; nevertheless, decarboxylation and crystallisation gave the desired hept-6-en-4-ynoic acid identical with that obtained from the acetoacetic ester reaction. The formation of a substantial proportion of substituted acetic acid when a propargylic halide is used in the acetoacetic ester ketone synthesis, with hydrolysis by aqueous alkali, appears likely to be general, for Gaudemar (*Compt. rend.*, 1953, **237**, 71) obtained equal amounts of hex-5-yn-2-one and pent-4-ynoic acid with propargyl bromide itself, while we have made a similar observation with but-2-ynyl chloride (Harper and Kazi, unpublished work).

As a further potential intermediate for subsequent chain extension by routes *B* or *E* (Crombie *et al.*, *loc. cit.*, 1950; Crombie, Harper, Stedman, and Thompson, *J.*, 1951, 2445),

hex-5-en-3-yn-1-ol (XVII) was prepared from ethylene oxide and sodiovinylacetylene in liquid ammonia.

The observations of Ferns and Lapworth (*J.*, 1912, **101**, 273), of Hückel *et al.* (*Annalen*, 1938, **533**, 1; 1939, **537**, 113; 1940, **543**, 191), and of Owen *et al.* (*J.*, 1949, 315, 320; 1950, 2103, 2108; 1952, 910; 1953, 404) that the toluene-*p*-sulphonates of saturated primary and secondary alcohols give rise to olefin by elimination with strongly basic reagents suggested that in the system $TsO{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}$ elimination, with concomitant formation of a conjugated diene, would be the preponderating reaction. The behaviour of the mono- and the di-toluene-*p*-sulphonate of *cis*-pent-2-ene-1 : 5-diol (XVIII), therefore, was examined as providing a possible route to *cis*-octa-5 : 7-dien-2-one (XIX) not requiring partial hydrogenation of an enyne system.

Semihydrogenation of an isolated acetylenic bond yields *cis*-ethylenes of higher purity than partial hydrogenation of an enyne. Pent-2-yne-1 : 5-diol was selectively hydrogenated over both palladised barium sulphate and palladised calcium carbonate (cf. Heuberger and Owen, *loc. cit.*) to the required *cis*-diol (XVIII). With 1 and 2 mols. of toluene-*p*-sulphonyl chloride in aqueous potassium hydroxide, this gave a liquid "ditoluene-*p*-sulphonate" (XX) and "monotoluene-*p*-sulphonate" that resisted purification. The "monotoluene-*p*-sulphonate" is considered to be predominantly (XXI) formed through more rapid reaction at the allylic hydroxyl group. Attempts to prepare the ditoluene-*p*-sulphonate in pyridine failed. This may be due to instability of the monotoluene-*p*-sulphonate in the presence of pyridine, ring closure occurring between the favourably disposed (*cis*-)hydroxyl and sulphonyloxy-groups, with the formation of 5 : 6-dihydro-2-pyran (XXII). While this work was in progress Haggis and Owen (*J.*, 1953, 391) recorded difficulty in preparing the ditoluene-*p*-sulphonate of 1 : 2-bishydroxymethyl*cyclo*hexane, showing that the monotoluene-*p*-sulphonate cyclised in the presence of pyridine to form 8-oxa[4 : 3 : 0]*bicyclo*nonane.

As for the ditoluene-*p*-sulphonate of pent-2-yne-1 : 5-diol, the crude ditoluene-*p*-sulphonate (XX) was treated with ethyl sodioacetoacetate and subjected to ketonic fission. Although analysis showed the steam-volatile ketonic product to have the formula $C_8H_{12}O$ expected for the octadienone (XIX), the ultraviolet (no absorption in the 227-mμ region) and infrared absorption (no conjugated vinyl absorption, acyclic α-saturated carbonyl 1708 cm.$^{-1}$) established the absence of a conjugated diene system. Furthermore, catalytic hydrogenation showed the presence of only one ethylenic bond. The product, therefore, was monocyclic and comparison of its physical properties and those of its derivatives (Table) with data for 4-acetyl*cyclo*hexene (XXIII) [Petrov, *J. Gen. Chem.* (*Russia*), 1941, **11**, 309; *Chem. Abs.*, 1941, **35**, 5873] pointed beyond doubt to their identity. It was evident that after

	4-Acetyl*cyclo*hexene	Our product
B. p.	80°/20 mm.	74°/16 mm.
n_D^{20}	1·4698	1·4697
Semicarbazone, m. p.	165—166°	168·5—169°
p-Nitrophenylhydrazone, m. p.	142—143°	141—143°
2 : 4-Dinitrophenylhydrazone, m. p.	—	148·5—149°

replacement of the allylic sulphonyloxy-group by acetoacetate anion the proximity of the β-sulphonyloxy-group, arising from the *cis*-configuration, favoured intramolecular replacement rather than elimination. Isolation of the total ketonic product by ether-extraction gave also a small amount of *cis*-8-hydroxyoct-5-en-2-one (XXIV) [infrared bands: hydroxyl 3425 (s), 1046 (s); unconjugated *cis*-CHR:CHR′ 1656 (w); α-saturated acyclic carbonyl, 1709 (s) cm.$^{-1}$; no absorption in the 970-cm.$^{-1}$ region (*trans*-CHR:CHR′)]. An identical ketone was prepared by semihydrogenation of 8-hydroxyoct-5-yn-2-one (XII) over palladised barium sulphate. The hydroxy-ketone (XXIV) presumably arose from the monotoluene-*p*-sulphonate (XXI) present as a contaminant in the crude ditoluene-*p*-sulphonate and in confirmation of this it was obtained in low yield, accompanied by 4-acetyl*cyclo*hexene, by reaction of the "monotoluene-*p*-sulphonate" of *cis*-pent-2-ene-1 : 5-diol with ethyl sodioacetoacetate followed by ketonic fission. These findings suggest that the "ditoluene-*p*-sulphonate" and the "monotoluene-*p*-sulphonate" were, in fact, mixtures of comparable composition.

The crude toluene-*p*-sulphonate (XXV) of *cis*-8-hydroxyoct-5-en-2-one (XXIV) was treated with ethanolic sodium ethoxide to effect elimination (and replacement), yielding *cis*-8-ethoxyoct-5-en-2-one (XXVI) [semicarbazone; infrared C–O stretching frequency for the alkyl ether, 1108 (vs) cm.$^{-1}$], and smaller amounts of desired *cis*-octa-5 : 7-dien-2-one (XIX) (semicarbazone, 2 : 4-dinitrophenylhydrazone; the infrared absorption showed a small peak at 1106 cm.$^{-1}$, probably owing to a trace of the ethoxy-ketone). The structure (XIX) was confirmed by the ultraviolet light absorption (max. at 228 mμ, ε 16,100), in agreement with a penta-2 : 4-*cis*-dienyl chromophore, and the infrared absorption spectrum [conjugated vinyl, 999 (s) and 910 (s) cm.$^{-1}$]. We consider this product to be stereochemically of high purity, but there was insufficient material for regeneration from the semicarbazone. Stereochemically slightly less pure diene-ketone was obtained in larger quantity by partial hydrogenation of oct-7-en-5-yn-2-one (unpublished experiments).

From the contrasting behaviour of the toluene-*p*-sulphonates of *cis*-8-hydroxyoct-5-en-2-one and 8-hydroxyoct-5-yn-2-one towards ethanolic sodium hydroxide it appears that there is a greater tendency for elimination to occur when the sulphonyloxy-group is β to an acetylenic bond than when it is β to an ethylenic bond.

(With R. J. D. Smith.) Although the condensation of 1 : 2-, 1 : 3-, and 1 : 4-dihalides with active methylene-containing compounds of the type of acetoacetic ester has often been used since the time of W. H. Perkin, jun., for the preparation of substituted *cyclo*propanes, *cyclo*butanes, and *cyclo*pentanes respectively (see Rodd, "Chemistry of Carbon Compounds," Vol. IIA, Elsevier Pub. Co., Amsterdam), the formation of substituted *cyclo*hexanes and *cyclo*heptanes from 1 : 5- and 1 : 6-dihalides has rarely been observed. The conformation of the longer polymethylene chains favours inter- rather than intra-molecular condensation. However, the ready formation of 4-acetyl*cyclo*hexene from *cis*-pent-2-ene-1 : 5-diol ditoluene-*p*-sulphonate (p. 129) suggested that the presence of a *cis*-ethylenic bond in the polymethylene chain induces a conformation more favourable to ring closure: in this case substituted *cyclo*heptenes and *cyclo*octenes might be accessible from the readily prepared higher homologues of *cis*-pent-2-ene-1 : 5-diol.

$$\underset{\text{(XXVII)}}{HO\cdot[CH_2]_n\cdot C{\equiv}CH} \longrightarrow \underset{\text{(XXVIII)}}{HO\cdot[CH_2]_n\cdot C{\equiv}C\cdot CH_2\cdot OH} \longrightarrow \underset{\text{(XXIX)}}{HO\cdot[CH_2]_n\cdot CH\overset{c}{=}CH\cdot CH_2\cdot OH}$$

Hydroxymethylation of pent 4-yn-1-ol and hex-5-yn-1-ol (XXVII; $n = 3$ and 4) by the formaldehyde–aqueous cuprous hydroxide method used for the lower homologue gave hex-2-yne-1 : 6-diol and hept-2-yne-1 : 7-diol (XXVIII; $n = 3$ and 4) in moderate yield. Semihydrogenation of these acetylenic diols over palladised barium sulphate then gave *cis*-hex-2-ene-1 : 6-diol and *cis*-hept-2-ene-1 : 7-diol (XXIX; $n = 3$ and 4).

As for *cis*-pent-2-ene-1 : 5-diol no crystalline ditoluene-*p*-sulphonate could be obtained from *cis*-hex-2-ene-1 : 6-diol and even under favourable conditions a liquid mixture of mono- and ditoluene-*p*-sulphonates was formed. A variety of methods (see Experimental section) was tried for the preparation of *cis*-1 : 6-dibromohex-2-ene before success was achieved by the method used by Johnson (*J.*, 1946, 1009) for but-2-yne-1 : 4-diol; even so the dibromide could not be purified by distillation.

Both the crude ditoluene-*p*-sulphonate and dibromide of *cis*-hex-2-ene-1 : 6-diol were treated under a variety of conditions with excess of ethyl sodioacetoacetate, but no definite ketonic product could be isolated. Experiments with *cis*-hept-2-ene-1 : 7-diol were therefore abandoned.

Experimental

Ultraviolet-light absorptions were determined for EtOH solutions by Mrs. A. I. Boston with a Hilger Medium Quartz Spectrograph. Infrared-light absorptions were determined partly with a Grubb Parsons single-beam spectrometer coupled to a Brown recorder and partly with a Grubb Parsons double-beam spectrometer, the pure liquids being used as capillary films.

p-Nitrophenylhydrazones and 2 : 4-dinitrophenylhydrazones were passed through a short column of alumina in benzene before final crystallisation. M. p.s are corrected.

But-3-yn-1-ol. By the procedure of *Inorg. Synth.*, 1946, **2**, 79, 128, sodium acetylide was prepared on a 12-molar scale in liquid ammonia and treated with a 10% excess of ethylene oxide to give but-3-yn-1-ol, b. p. 125—130°, n_D^{20} 1·438—1·441, in 42% yield (average of many runs) (cf. Hennion and Murray, *J. Amer. Chem. Soc.*, 1942, **64**, 1220; Campbell, Campbell, and Eby, *ibid.*, 1938, **60**, 2882).

Pent-2-yne-1 : 5-diol.—By a procedure similar to that of Heuberger and Owen (*J.*, 1952, 910; cf. Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586) on a 0·75-molar scale, but-3-yn-1-ol was converted into pent-2-yne-1 : 5-diol, b. p. 107°/0·25 mm., n_D^{20} 1·488—1·489, in 66% yield. Like Heuberger and Owen we had found that interaction of the Grignard reagent from but-3-yn-1-ol with paraformaldehyde gave a lower yield of pent-2-yne-1 : 5-diol.

Pent-2-yne-1 : 5-diol Ditoluene-p-sulphonate.—To a stirred solution of pent-2-yne-1 : 5-diol (20 g., 0·2 mole) and toluene-*p*-sulphonyl chloride (78 g., 0·4 mole) in acetone (150 ml.), kept at 10°, aqueous potassium hydroxide (33·6 g. in 60 ml.) was added dropwise during 1 hr. After further stirring at room temperature overnight, water was added. Ether-extraction followed by drying ($MgSO_4$) and evaporation then gave an oil which slowly but incompletely crystallised (60 g., 73% average yield). Trituration with methanol followed by crystallisation from methanol, gave *pent-2-yne-1 : 5-diol ditoluene-p-sulphonate*, m. p. 58° (Found : C, 55·1; H, 5·1; S, 16·1. $C_{19}H_{20}O_6S_2$ requires C, 55·85; H, 4·95; S, 15·7%). Crude ditoluene-*p*-sulphonate was used in the following experiments.

(*a*) Ditoluene-*p*-sulphonate (16·3 g., 0·04 mole) was added in portions with ethanol (20 ml.) to a solution of sodium ethoxide (from sodium, 2·3 g.) in ethanol (60 ml.). When the initial reaction had subsided the mixture was heated on the steam-bath under reflux for 30 min. and then most of the alcohol was boiled off. Addition of water to the paste and ether-extraction, followed by drying ($MgSO_4$) at 5° in the presence of quinol, and distillation, gave *1-ethoxypent-4-en-2-yne* (0·81 g., 20%), b. p. 83—85°/100 mm., n_D^{20} 1·458 (Found : C, 76·3; H, 9·25. $C_7H_{10}O$ requires C, 76·3; H, 9·15%), possessing a celery-like odour. Light absorption : max. at 229 mμ (ε 9000). The unprotected ether polymerised within a few days at room temperature. Distillation of the residue gave a fraction (0·56 g.), b. p. 115—118°/15 mm., n_D^{20} 1·463 (Found : C, 67·1; H, 9·85. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4. Calc. for $C_9H_{16}O_2$: C, 69·2; H, 10·3%).

(*b*) Ditoluene-*p*-sulphonate (25 g.) was added during 15 min. to a hot solution of potassium hydroxide (10 g.) in 50% aqueous ethanol (20 ml.) containing a trace of Teepol detergent. After a further 15 minutes' heating under reflux steam-distillation followed by extraction of the distillate as in (*a*) and distillation gave 1-ethoxypent-4-en-2-yne (0·90 g., 13%), b. p. 80—82°/85 mm., n_D^{20} 1·459. A higher-boiling fraction (0·45 g.) had b. p. 104—112°/13 mm., n_D^{20} 1·494—1·505, and probably contained dipent-4-en-2-ynyl ether.

(*c*) Ditoluene-*p*-sulphonate (25 g.) was added in portions to a stirred boiling solution of potassium hydroxide (10 g.) in water (25 ml.) containing a trace of Teepol detergent with simultaneous distillation. Finally the mixture was steam-distilled, to give an oil which rapidly discoloured in air (quinol was added to prevent this). Saturation of the distillate with salt, extraction with ether, drying as in (*a*), and distillation gave (i) pent-4-en-2-yn-1-ol (0·22 g., 5%), b. p. 72°/15 mm., n_D^{20} 1·493, and (ii) *dipent-4-en-2-ynyl ether* (0·76 g., 17%), b. p. 106°/12 mm., n_D^{20} 1·520—1·5215 (Found : C, 81·0; H, 7·05. $C_{10}H_{10}O$ requires C, 82·1; H, 6·9%). The pent-4-en-2-yn-1-ol gave a phenylurethane, needles [from light petroleum (b. p. 80—100°)], m. p. 80·5—81°, raised to 80·5—81·5° on admixture with the specimen described on p. 132.

(*d*) Ditoluene-*p*-sulphonate (40·8 g., 0·1 mole) was added during 5 min. to a stirred hot solution of ethyl sodioacetoacetate (0·2 mole) in ethanol. After a further hour's stirring and heating under reflux most of the ethanol was distilled off. The residue was stirred with 5% aqueous sodium hydroxide (200 ml.) at room temperature overnight. Next day a little oil was removed, the alkaline solution acidified to methyl-orange with concentrated hydrochloric acid and warmed to 50° to bring about decarboxylation. An oil separated. Steam-distillation, saturation of the distillate with salt, extraction with ether, and washing of the extract with sodium hydrogen carbonate solution, followed by drying as in (*a*) and distillation, gave *oct-7-en-5-yn-2-one* (0·85 g., 7%), b. p. 84—89°/15 mm., n_D^{20} 1·475—1·478. A much larger amount of oil was not steam-volatile but was not examined; it probably contained 8-hydroxyoct-5-yn-2-one. Oct-7-en-5-yn-2-one gave a semicarbazone, m. p. 142°, raised to 142·0—142·5° on admixture with the specimen described on p. 133, and a 2 : 4 dinitrophenylhydrazone, m. p. 80·0—80·7°, raised to 81° on admixture with the specimen described on p. 133.

Pent-2-yne-1 : 5-diol Monotoluene-p-sulphonate.—To a stirred ice-cooled solution of pent-2-yne-1 : 5-diol (20 g., 0·2 mole) and toluene-*p*-sulphonyl chloride (39 g., 0·2 mole) in acetone (100 ml.), aqueous potassium hydroxide (16·8 g. in 30 ml.) was added slowly. Then, by the procedure

used for the ditoluene-*p*-sulphonate, pent-2-yne-1 : 5-diol monotoluene-*p*-sulphonate (36·5 g.) was obtained as a yellow oil and stored at 5°. This crude monotoluene-*p*-sulphonate was used in the following experiments.

(*e*) Monotoluene-*p*-sulphonate (7·7 g.) in ethanol (10 ml.) was added to a solution of sodium ethoxide (from sodium, 0·85 g.) in ethanol (10 ml.). Then, proceeding as in (*a*), distillation gave *5-ethoxypent-3-yn-1-ol* (1·28 g., 24% overall yield from pentynediol), b. p. 107—113°/9 mm., mainly 112°, n_D^{20} 1·463—1·4605 (Found : C, 65·9; H, 9·25. $C_7H_{12}O_2$ requires C, 65·6; H, 9·4%), preceded by a forerun (0·16 g.), b. p. up to 50°/10 mm., n_D^{20} 1·459, probably largely 1-ethoxypent-4-en-2-yne.

(*f*) Monotoluene-*p*-sulphonate (107 g., 0·42 mole) dissolved in ethanol (120 ml.) was added during 90 min. to a stirred boiling solution of ethyl sodioacetoacetate (0·4 mole) in ethanol (240 ml.) under reflux. Then, proceeding as in (*d*) and with 5% aqueous sodium hydroxide (400 ml.), the acid solution after decarboxylation was made alkaline (to pH 9), saturated with salt, extracted with ether, and the extract was dried (Na_2SO_4) and concentrated. Distillation then gave (i) oct-7-en-5-yn-2-one (4·16 g., 5·5% overall yield from pentynediol), b. p. 75—79°/7 mm., n_D^{20} 1·478—1·481, and (ii) *8-hydroxyoct-5-yn-2-one* (7·63 g., 10% overall yield), b. p. 104—110°/0·2 mm., mainly 107°, n_D^{20} 1·479—1·481 (Found : C, 68·15; H, 8·5. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%). Oct-7-en-5-yn-2-one gave a semicarbazone, m. p. 140·5—141·5°, not depressed on admixture with the specimens described below and on p. 133. The *semicarbazone of* 8-hydroxyoct-5-yn-2-one was prepared in aqueous solution and recrystallised from water; it formed transparent plates, m. p. 141·5—142·5° (Found : C, 54·95; H, 7·6. $C_9H_{15}O_2N_3$ requires C, 54·8; H, 7·65%); the yellow 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol as needles, m. p. 111—112° (Found : C, 52·5; H, 4·95. $C_{14}H_{16}O_5N_4$ requires C, 52·5; H, 5·05%).

8-Hydroxyoct-5-yn-2-one (1·12 g.) and toluene-*p*-sulphonyl chloride (1·55 g.) were shaken in acetone (4 ml.) at room temperature whilst aqueous potassium hydroxide (0·67 g. in 2 ml.) was added during 90 min. After a further 2 hours' shaking the crude toluene-*p*-sulphonate (1·85 g.) was isolated as for the ditoluene-*p*-sulphonate above and to it sodium ethoxide (from sodium, 0·37 g.) in ethanol (12 ml.) was added. Then, proceeding as in (*a*), distillation finally gave oct-7-en-5-yn-2-one (0·37 g., 38% yield from hydroxy-ketone), b. p. 76—80°/7 mm., n_D^{20} 1·481. The semicarbazone had m. p. 141·5—142·5°, not depressed on admixture with the specimens described above and on p. 133.

In another experiment the crude toluene-*p*-sulphonate from 8-hydroxyoct-5-yn-2-one (1·12 g.) was boiled under reflux with potassium hydroxide (2·5 g.) in 50% aqueous ethanol (5 ml.) for 30 min. Steam-distallation and addition of Brady reagent to the first 20 ml. of distillate gave impure oct-7-en-5-yn-2-one 2 : 4-dinitrophenylhydrazone (0·56 g., 27%), m. p. 77—78° after crystallisation, raised on admixture with the specimen described on p. 133.

Vinylacetylene.—By the procedure of Eglington and Whiting (*J.*, 1950, 3650) and on a similar scale, but-3-yn-1-ol was converted into the crude toluene-*p*-sulphonate and thence into vinylacetylene, which on redistillation was obtained in 75—80% overall yield. The use of a technical grade of pyridine in the preparation of the toluene-*p*-sulphonate resulted in tar formation and a reduced yield. Invariably, on redistillation of the vinylacetylene, a small amount of less volatile liquid was left in the first trap, perhaps 1-ethoxybut-3-yne formed by a replacement reaction.

Pent-4-en-2-yn-1-ol.—Redistilled vinylacetylene (41 g., 1 mol.) in cooled ether (240 ml.) was slowly added to a stirred ice-cooled Grignard solution prepared from ethyl bromide (88 g., 1 mol.) and magnesium (19·4 g.) in ether (240 ml.) under a solid carbon dioxide–ethanol reflux condenser. After the addition the reaction mixture was boiled for 3 hr., then cooled, and dried paraformaldehyde (36 g., 1·5 mol.) was sublimed in a stream of nitrogen on to the stirred surface of the solution, causing gentle boiling. The resinous complex was decomposed by the addition of dilute sulphuric acid with cooling, and the ethereal solution separated, washed, dried (Na_2SO_4), and concentrated. Distillation then gave pent-4-en-2-yn-1-ol (32 g., 50%), b. p. 67·5°/16 mm., 58°/12 mm., n_D^{20} 1·4940 (Found : C, 73·45; H, 7·25. Calc. for C_5H_6O : C, 73·15; H, 7·35%). Microhydrogenation : 3·0 mol. uptake. Light absorption : max. at 227 mμ (ε 12,000). The phenylurethane formed needles, m.p. 82·5°, from light petroleum. The alcohol formed a gel at room temperature during 14 days. Nazarov and Torgov (*Chem. Abs.*, 1948, **42**, 7735g) prepared pent-4-en-2-yn-1-ol (described as " vinylethinylcarbinol ") by a similar method in 65% yield but used a 30% excess of vinylacetylene.

Pent-4-en-2-ynyl Chloride.—On a 0·5—1·0-molar scale and by the procedure used for *trans*-penta-2 : 4-dien-1-ol (Part VII, *J.*, 1951, 2906), pent-4-en-2-yn-1-ol was converted into *pent-4-en-2-ynyl chloride* (55—60%), b. p. 60°/65 mm., n_D^{20} 1·5505 (Found : Cl, 35·5. C_5H_5Cl requires Cl, 35·1%). It was necessary to add a Silicone antifoaming agent before distillation of the chloride.

The distilled chloride darkened quickly even at 0° but a solution in light petroleum with a trace of quinol was stable at this temperature.

Oct-7-en-5-yn-2-one.—By the procedure recorded in Part VII (*loc. cit.*) for *trans*-oct-5-en-7-yn-2-one, on a 0·25-molar scale, pent-4-en-2-ynyl chloride was converted into *oct-7-en-5-yn-2-one* (29—31% yield), b. p. 87—90°/16 mm., 75°/7 mm., n_D^{20} 1·4805 (Found : C, 78·4; H, 8·2. $C_8H_{10}O$ requires C, 78·6; H, 8·25%). Light absorption : max. at 222 and 232 mμ (ε 12,200 and 11,000). The ketone could be stored without deterioration in the presence of quinol at 0°. The *semicarbazone* of oct-7-en-5-yn-2-one formed plates (from ethanol), m. p. 141·5° (Found : C, 59·9; H, 7·35. $C_9H_{13}ON_3$ requires C, 60·3; H, 7·3). The 2 : 4-*dinitrophenylhydrazone* was obtained first as red plates (from ethanol), m. p. 67·5° (Found : C, 54·6; H, 4·7; N, 18·6. $C_{14}H_{14}O_4N_4$ requires C, 55·6; H, 4·7; N, 18·55%), and later as orange needles, m. p. 81° (Found : C, 55·5; H, 4·5%); a mixed m. p. of the two forms was 76—77·5°.

On hydrogenation in ethanol over Adams catalyst oct-7-en-5-yn-2-one (106 mg.) absorbed 2·90 mols. of hydrogen. Filtration and treatment of the hot solution with 2 : 4-dinitrophenylhydrazine and a drop of concentrated hydrochloric acid gave octan-2-one 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 58°.

Hept-6-en-4-ynoic Acid.—Overnight the cold residue from the steam-distillation above deposited crystals. These were taken up in ether and shaken with aqueous sodium hydrogen carbonate. This alkaline extract was combined with the sodium hydrogen carbonate washings of the ether extract of the steam-distillate and acidified, *hept-6-en-4-ynoic acid* (20%) separating. On recrystallisation from water or from light petroleum (b. p. 40—60°) at 0° the acid formed plates, m. p. 57·5° (Found : C, 67·7; H, 6·65. $C_7H_8O_2$ requires C, 67·75; H, 6·5%). Coloured impurities which could not be removed with activated carbon were removed by warming in solution with silica gel. Light absorption : max. at 224 and 233 mμ (ε 11,300 and 10,400). The acid was light-sensitive and unstable but in a refrigerator in a vacuum or under water or light petroleum could be stored without deterioration. The p-*bromophenacyl ester* formed plates (from aqueous ethanol), m. p. 99·5—100·5° (Found : C, 55·6; H, 4·1. $C_{15}H_{13}O_3Br$ requires C, 56·0; H, 4·1%).

On hydrogenation in ethyl acetate over 5% palladised barium sulphate hept-6-en-4-ynoic acid (0·50 g.) absorbed 3·0 mols. of hydrogen. Distillation then gave heptanoic acid (0·36 g., 72%), b. p. 121—123°/20 mm., n_D^{20} 1·4245, characterised as the *p*-bromophenacyl ester, m. p. 70·2—71·2°, in agreement with literature data.

Pent-4-en-2-ynyl chloride (5·5 g.) was added to a stirred boiling solution of ethyl sodiomalonate (0·05 mole) in ethanol. By proceeding in the usual way the undistilled malonic ester (9·6 g.) was hydrolysed with aqueous sodium hydroxide, and the malonic acid (6·2 g.) isolated with ether. Recrystallised from benzene the *acid* was microcrystalline with no m. p. but sintering above 140° (Found : C, 60·7; H, 4·9. $C_8H_8O_4$ requires C, 57·2; H, 4·8. $C_{13}H_{21}O_4$ requires C, 67·2; H, 5·2%). The acid decomposed in a few days at room temperature. The acid (3 g.) was heated at 140—150° for 2·5 hr. and the brown sintered mass thoroughly extracted with light petroleum (b. p. 40—60°), to give crude hept-6-en-4-ynoic acid (0·80 g.) which after repeated crystallisation from light petroleum had m. p. and mixed m. p. 57°.

Hex-5-en-3-yn-1-ol.—By the procedure of *Inorg. Synth.*, 1946, **2**, 128, sodamide was prepared from sodium (4·5 g.) in liquid ammonia (250 ml.), and cooled vinylacetylene (9·5 g.) added all at once in a little ether. After 40 minutes' stirring ethylene oxide (20 ml.) was added and stirring continued for 48 hr. After a further 36 hr. ether and ammonium chloride were added, followed by water. After thorough ether-extraction the extracts were washed, dried (Na_2SO_4), and distilled, to give *hex-5-en-3-yn-1-ol* (2·7 g.), b. p. 73—81°/12 mm., n_D^{20} 1·4975—1·4980 (Found : C, 74·95; H, 8·55. C_6H_8O requires C, 75·0; H, 8·4%). Microhydrogenation : 3·1 mols. uptake. Light absorption : max. at 226 mμ (ε 11,700).

cis-*Pent-2-ene-1 : 5-diol.*—On a 1-molar scale pent-2-yne-1 : 5-diol was hydrogenated in ethyl acetate at room temperature and atmospheric pressure over 5% palladised barium sulphate or palladised calcium carbonate until 1 mol. of hydrogen was absorbed. Filtration and distillation then gave *cis*-pent-2-ene-1 : 5-diol, b. p. 84°/0·1 mm., 91—92°/0·4 mm., n_D^{20} 1·4763—1·4769, in 80—85% yield.

cis-*Pent-2-ene-1 : 5-diol "Ditoluene-p-sulphonate."*—By the procedure used to prepare pent-2-yne-1 : 5-diol ditoluene-*p*-sulphonate (p. 131), *cis*-pent-2-ene-1 : 5-diol (10·2 g., 0·1 mole) was converted into a "ditoluene-*p*-sulphonate" (21 g.), obtained as an oil (Found : C, 54·5; H, 6·2; S, 13·6. $C_{19}H_{22}O_6S_2$ requires C, 55·6; H, 5·35; H, 5·35; S, 15·6. $C_{12}H_{16}O_4S$ requires C, 56·25; H, 6·25; S, 12·5%). This crude "ditoluene-*p*-sulphonate" was used in the following experiments.

(*g*) "Ditoluene-*p*-sulphonate" from 0·1 mole of diol was added to ethyl sodioacetoacetate

(0·08 mole) at 50—55° and the reaction completed at this temperature. Then, proceeding as in (*d*), distillation finally gave 4-acetyl*cyclo*hexene (1·33 g., 11% overall yield from diol), b. p. 69—74°/17 mm., which was converted into the semicarbazone and this was recrystallised from ethanol (Found: C, 59·8; H, 8·4. Calc. for $C_9H_{13}ON_3$: C, 59·7; H, 8·35%). Regeneration from the semicarbazone with hot aqueous oxalic acid gave pure 4-acetyl*cyclo*hexene (Found: C, 76·7; H, 9·8. Calc. for $C_8H_{12}O$: C, 77·35; H, 9·75%). The *p*-nitrophenylhydrazone formed yellow needles from ethanol (Found: C, 64·4; H, 6·8. Calc. for $C_{14}H_{17}O_2N_3$: C, 64·8; H, 6·6%), and the 2:4-*dinitrophenylhydrazone* orange-red laths (Found: C, 55·5, 55·3; H, 5·55, 5·75; N, 18·65. $C_{14}H_{16}O_4N_4$ requires C, 55·3; H, 5·3; N, 18·4%). For physical properties of the ketone and its derivatives see Table (p. 129).

On hydrogenation in ethyl acetate over 5% palladised barium sulphate 4-acetyl*cyclo*hexene (220 mg.) absorbed 1·0 mol. of hydrogen in 5 min.

In another condensation on the same scale but with 0·1 mole of ethyl sodioacetoacetate and isolation by ether-extraction after decarboxylation, distillation gave 4-acetyl*cyclo*hexene (2·21 g., 18% overall yield from diol), b. p. 64—70°/7 mm., n_D^{20} 1·4675—1·4682, and *cis*-8-hydroxyoct-5-en-2-one (1·06 g., 7·5% overall yield from diol), b. p. 88—93°/0·07 mm., n_D^{20} 1·466—1·467.

cis-*Pent*-2-*ene*-1:5-*diol "Monotoluene*-p-*sulphonate."*—By the procedure used to prepare pent-2-yne-1:5-diol monotoluene-*p*-sulphonate (p. 131), *cis*-pent-2-ene-1:5-diol (20·4 g., 0·2 mole) was converted into a "monotoluene-*p*-sulphonate" (24 g.), obtained as in an oil. This crude "monotoluene-*p*-sulphonate" was used in the following experiments.

(*h*) "Monotoluene-*p*-sulphonate" from 0·2 mole of diol was caused to react with ethyl sodioacetoacetate (0·09 mole) as in (*f*). Continuing as in (*f*), distillation finally gave 4-acetyl*cyclo*hexene (1·67 g., 7% overall yield from diol), b. p. 72—73°/13 mm., n_D^{20} 1·469, and cis-8-*hydroxyoct*-5-*en*-2-*one* (1·57 g., 6% overall yield from diol), b. p. 93—96°/0·08 mm., n_D^{20} 1·465—1·469, mainly 1·4684 (Found: C, 67·9; H, 10·25. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%). A semicarbazone of *cis*-8-hydroxyoct-5-en-2-one could not be obtained; the 2:4-*dinitrophenylhydrazone*, formed in only poor yield, was sparingly soluble in ethanol but, crystallised from ethyl acetate, had m. p. 203—204·5° (Found: C, 52·8; H, 5·2. $C_{14}H_{18}O_5N_4$ requires C, 52·2; H, 5·6%). The 4-acetyl*cyclo*hexene formed a semicarbazone, m. p. and mixed m. p. 169°.

8-Hydroxyoct-5-yn-2-one (4·20 g.) was hydrogenated in ethyl acetate over 5% palladised barium sulphate (0·25 g.). Uptake was interrupted when 1 mol. of hydrogen had been absorbed although no change in rate was observed. Filtration and distillation then gave *cis*-8-hydroxyoct-5-en-2-one (3·32 g., 78%), b. p. 85—88°/0·03 mm. (mainly 86°), n_D^{20} 1·468—1·469.

cis-*Octa*-5:7-*dien*-2-*one.*—By the procedure for the conversion of 8-hydroxyoct-5-yn-2-one into oct-7-en-5-yn-2-one, *cis*-8-hydroxyoct-5-en-2-one (3·58 g.) was converted into the crude toluene-*p*-sulphonate (5·1 g.) and to it sodium ethoxide (from sodium, 0·69 g.) in ethanol (25 ml.) was added. Then, proceeding as in (*a*), distillation finally gave (i) cis-*octa*-5:7-*dien*-2-*one* (0·34 g., 16% overall yield from hydroxy-ketone), b. p. 78—82°/9 mm., 70—72°/6 mm. on redistillation, n_D^{20} 1·470, 1·473 after redistillation (Found: C, 76·65; H, 9·6. $C_8H_{12}O$ requires C, 77·4; H, 9·75%), and (ii) cis-8-*ethoxyoct*-5-*en*-2-*one* (0·60 g., 21% overall yield from the hydroxy-ketone), b. p. 109—112°/7 mm., 106—107°/7 mm. on redistillation, n_D^{20} 1·451—1·448, 1·446 after redistillation (Found: C, 70·7; H, 10·65. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·65%).

The infrared spectrum of *cis*-octa-5:7-dien-2-one was identical with that of a specimen obtained by another route (Part XI), except for a small band at 1106 cm.$^{-1}$ due to a trace of *cis*-8-ethoxyoct-5-en-2-one. The semicarbazone of *cis*-oct-5:7-dien-2-one crystallised from aqueous ethanol as plates, m. p. 115·0—115·5°, and the 2:4-dinitrophenylhydrazone, purified by crystallisation from ethanol, had m. p. 52·5—53·5°. These derivatives were identical (mixed m. p.) with those described in Part XI, where analytical data will be given.

The *semicarbazone* of *cis*-8-ethoxyoct-5-en-2-one crystallised from aqueous ethanol as plates, m. p. 98° (Found: C, 57·8; H, 9·4. $C_{11}H_{21}O_2N_3$ requires C, 58·1; H, 9·3%).

cis-*Hex*-2-*ene*-1:6-*diol.*—Tetrahydrofurfuryl alcohol was converted into tetrahydrofurfuryl chloride on a 6-mole scale by the procedure of *Org. Synth.* (1945, **25**, 84) in 58—78% yield and thence into pent-4-yn-1-ol on a 2-molar scale by a procedure similar to that of Eglington, Jones, and Whiting (*J.*, 1952, 2873; Stokes, unpublished work) in up to 85% yield. In the latter stage, when technical instead of pure dry ammonium chloride was used to decompose the sodium salts, the yield of pent-4-yn-1-ol dropped considerably. Even so this ring scission with sodamide in liquid ammonia is erratic and one run gave pent-4-en-1-ol (75%), b. p. 47—50°/11 mm., n_D^{20} 1·4322, as the product perhaps owing to incomplete conversion of the sodium into sodamide.

By the procedure used for pent-2-yne-1:5-diol (p. 131), on a 0·5—2·0-molar scale and with a reaction time of 24 hr. at 100°, pent-4-yn-1-ol was converted into hex-2-yne-1:6-diol, b. p.

131°/0·65 mm., 115°/0·1 mm., n_D^{20} 1·487 (Found, C, 62·7; H, 8·85. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·85%), in up to 41% yield. Hex-2-yne-1 : 6-diol has since been prepared in a similar way by Paul and Tchelitcheff (*Bull. Soc. chim. France*, 1953, 417). The yield of diol appeared to decrease with increase in the scale of preparation. Hydrogenation of hex-2-yne-1 : 6-diol in ethyl acetate over 5% palladised barium sulphate on a 0·5-molar scale then gave cis-*hex-2-ene*-1 : 6-*diol* (up to 85%), b. p. 108°/0·25 mm., 89°/0·06 mm., n_D^{20} 1·473—1·476 (Found : C, 62·0; H, 10·6. $C_6H_{14}O_2$ requires C, 62·0; H, 10·4%). No crystalline derivatives could be obtained from this diol.

By the procedure used for pent-2-yne-1 : 5-diol, *cis*-hex-2-ene-1 : 6-diol (1 mol.) and toluene-*p*-sulphonyl chloride (2 mol.) in acetone were treated with aqueous potassium hydroxide to give an oil, considered to be a mixture of the mono- and di-toluene-*p*-sulphonate, from which no more than a trace of crystals could be isolated.

cis-1 : 6-*Dibromohex-2-ene*.—No dibromide was obtained by reaction of *cis*-hex-2-ene-1 : 6-diol with phosphorus tribromide at 0—20° in either the presence or absence of pyridine, or with 48% hydrobromic acid and cuprous bromide. A little dibromide (up to 12% yield) was obtained with 48% hydrobromic acid and sulphuric or toluene-*p*-sulphonic acid.

A satisfactory product was obtained by addition of phosphorus tribromide (27 g.) to a vigorously stirred suspension of *cis*-hex-2-ene-1 : 6-diol (11·6 g.) in benzene (100 ml.) at room temperature during 1 hr. Iced water was then added and the benzene layer separated, washed, and evaporated under reduced pressure without heating, to give cis-1 : 6-*dibromohex-2-ene* (15 g., 65%), n_D^{20} 1·527 (Found : Br, 63·0. $C_6H_{10}Br_2$ requires Br, 66·0%). Decomposition invariably ensued on attempted distillation.

cis-*Hept-2-ene*-1 : 7-*diol*.—The following preparation of tetrahydropyranylmethyl chloride devised by Mr. B. J. Stokes was preferred to that of Eglington, Jones, and Whiting (*loc. cit.*) : Thionyl chloride (130 g.) was added during 30 min. to a stirred mixture of tetrahydropyranylmethanol (116 g.) and pure pyridine (113 g.) heated in an oil-bath at 135°. After a further 2 hours' heating the cooled pasty mass was repeatedly extracted with ether. The combined ether extracts were washed, dried, and distilled, to give tetrahydropyranylmethyl chloride (up to 68%), b. p. 56—57°/15 mm., n_D^{20} 1·4617 (Found : C, 53·6; H, 8·4. Calc. for $C_6H_{11}OCl$: C, 53·6; H, 8·3%). Eglington, Jones, and Whiting obtained a 48% yield by reaction at 0° during 16 hr. Ring scission of tetrahydropyranylmethyl chloride by a procedure similar to that of these authors (*loc. cit.*; Stokes, unpublished work) on a 1-molar scale gave hex-5-yn-1-ol, b. p. 73—75°/15 mm., n_D^{20} 1·4502, in 88% yield.

By the procedure used for hex-2-yne-1 : 6-diol and on a 0·5-molar scale, hex-5-yn-1-ol was converted into *hept-2-yne*-1 : 7-*diol* (38%, one experiment only), b. p. 133°/1·0 mm., 105°/0·05 mm., n_D^{20} 1·4827 (Found : C, 64·45; H, 9·15. $C_7H_{12}O_2$ requires C, 65·5; H, 9·4%).

Hept-2-yne-1 : 7-diol (5·9 g.) was hydrogenated in methanol over 5% palladised barium sulphate (0·2 g.) until 0·98 mol. of hydrogen was absorbed. Interruption of the hydrogenation, filtration, and distillation then gave cis-*hept-2-ene*-1 : 7-*diol* (4·7 g., 81%), b. p. 105—106°/0·25 mm., n_D^{20} 1·4708 (Found : C, 64·2; H, 11·0. $C_7H_{14}O_2$ requires C, 64·6; H, 10·8%).

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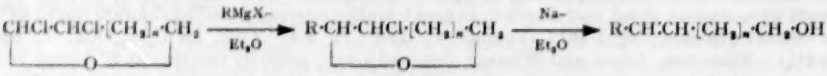
26. *Stereochemical Studies of Olefinic Compounds. Part V.* Further Observations on the Ring Fission of 3-Chlorotetrahydro-furans and -pyrans.*

By L. Crombie, (Mrs.) J. Gold, S. H. Harper, and B. J. Stokes.

Chlorination of tetrahydrofuran and tetrahydropyran yields *trans*-2 : 3-dichlorotetrahydrofuran and *trans*-2 : 3-dichlorotetrahydropyran, identical with the compounds obained by adding chlorine to 2 : 3-dihydrofuran and 3 : 4-dihydropyran respectively. The configurations assigned to the two stereoisomers of the 2-alkyl-3-chlorotetrahydrofurans on the basis of the Auwers–Skita rules are supported by comparison of their speeds of dehydrochlorination with sodium ethoxide. Quantitative infrared analyses of the *cis-trans* mixtures of pent-3-en-1-ols and hex-3-en-1-ols formed on sodium ring fission of *cis*- and *trans*-3-chloro-2-methyl- and -ethyl-tetrahydrofurans are reported.

Some reactions of 3-chlorotetrahydro-furans and -pyrans are reported.

Fission of β-halogeno-ethers with electropositive metals is a valuable general reaction for the introduction of an olefinic linkage and many aspects of this reaction have now been examined. We have been especially interested in it as a method for chain extension by schemes outlined in Parts II and III (Crombie and Harper, *J.*, 1950, **1707**, **1714**). These involve treating an alkylmagnesium halide with 2 : 3-dichlorotetrahydro-furan or -pyran (I, $n = 1$ or 2) and ring fission of the 2-alkyl-3-chloro-intermediate (II) with sodium to give an alk-3-en-1-ol or an alk-4-en-1-ol (III; $n = 1$ or 2). The present contribution is concerned with both the intermediates and the fission products.



(I) (II) (III)

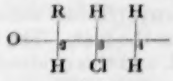
The starting materials for chain extension by four or five carbon atoms are normally the dichloro-compounds (I; $n = 1$ or 2), though for the latter Brandon, Derfer, and Boord (*J. Amer. Chem. Soc.*, 1950, **72**, 2120) have used 2 : 3-dibromotetrahydropyran. However, this gives less stable products and inferior yields (cf. Parham and Holmquist, *ibid.*, 1954, **76**, 1173). 2 : 3-Dichlorotetrahydropyran is best prepared by addition of chlorine to 3 : 4-dihydropyran and this type of addition is generally recognised as *trans* (Barton and Miller, *ibid.*, 1950, **72**, 1067; references cited by Crombie and Harper, *J.*, 1950, 1714). On the other hand 2 : 3-dichlorotetrahydrofuran is best prepared by chlorination of tetrahydrofuran in presence of an iodine catalyst. Its geometrical configuration has been unknown. Both dichloro-compounds are homogeneous, as judged by their behaviour on distillation. We have now prepared 2 : 3-dichlorotetrahydropyran by chlorination of tetrahydropyran under conditions which correspond to those used for the chlorination of tetrahydrofuran and, correspondingly, 2 : 3-dichlorotetrahydrofuran by addition of chlorine to dihydrofuran. Infrared absorption spectra show the two dichlorotetrahydrofurans and the two dichlorotetrahydropyrans to be severally identical, thus demonstrating that the chlorination (substitution), whatever its mechanism, yields a *trans*-product. Samples of dihydrofuran for this work were originally prepared by β-halogeno-ether cleavage from 3-chloro-2-ethoxytetrahydrofuran (Normant, *Compt. rend.*, 1949, **228**, 102); of the two ether linkages present the exocyclic one is ruptured at a greater speed than the cyclic one. However, it was difficult to obtain the dihydrofuran pure enough, so eventually the material was prepared by Paul, Fluchaire, and Collardeau's isomerisation method (*Bull. Soc. chim. France*, 1950, **668**).

2 : 3-Dichlorotetrahydrofuran with methyl-, ethyl-, *iso*propyl-, and *tert.*-butyl-magnesium halides yielded the four corresponding 2-alkyl-3-chlorotetrahydrofurans and these were fractionally distilled to give specimens of the *cis*- and *trans*-isomers of the first

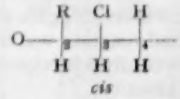
* Part IV, *J.*, 1955, 1512.

three compounds. (The *tert.*-butyl isomers decomposed rapidly on distillation and fractionation was impossible.) Although specimens of the three pairs of isomers were obtained, resolution of the mixtures was not complete with the helices-packed column employed. Nevertheless it was possible to estimate, by refractometric analysis of the intermediate fractions, that the 3-chlorotetrahydro-2-methylfuran and 3-chloro-2-ethyltetrahydrofuran contained approximately 35% of the lower-boiling *trans*-isomer, whilst the 3-chloro-2-*iso*propyltetrahydrofuran contained about 50% of the *trans*-isomer. Inversion at $C_{(2)}$ is thus somewhat reduced with the larger incoming alkyl group.

Assignment of configurations to the above compounds is based upon the Auwers–Skita rules which are likely to be valid in this and the corresponding 2-alkyl-3-chlorotetrahydropyran series (for information on the scope of the rules, see Haggis and Owen, *J.*, 1953, 408). Substantiation comes from the rates of dehydrochlorination of the three pairs of isomers (II; $n = 1$, R = Me, Et, and Pr^i) with ethanolic sodium ethoxide. The three lower-boiling isomers reacted at almost the same speed whereas the three higher-boiling isomers reacted considerably faster, the rate increasing in the order $Pr^i < Et < Me$. In the *trans*-isomer, a *trans*-elimination of hydrogen chloride is possible only between $C_{(3)}$ and $C_{(4)}$, whereas in the *cis*-isomer a similar *trans*-elimination is possible between $C_{(3)}$ and $C_{(2)}$ as well as between $C_{(3)}$ and $C_{(4)}$, and it can be deduced from Normant's results (*Compt. rend.*, 1948, **227**, 283) that a hydrogen atom at $C_{(2)}$ is more reactive than one at $C_{(4)}$.



trans



cis

If it is conceded that *trans*-elimination is highly probable in this reaction and in a system of this type, these experiments reinforce the assignments of configuration made above. It is of interest that Riobé [*Ann. Chim.* (*France*), 1949, **4**, 593] has shown that in parallel eliminations in the 2-alkyl-3-chlorotetrahydropyran series the lower-boiling isomers (II; $n = 2$, R = Et, Pr^n, and Bu^n) react at the same speed, whilst that with R = Me is rather slower. All four higher-boiling isomers react faster than any of the lower-boiling ones and in the order $Bu^n = Pr^n < Et < Me$.

It was found qualitatively (Crombie and Harper, *loc. cit.*) that, whereas both *cis*- and *trans*-2-alkyl-3-chlorotetrahydropyrans yield *trans*-alk-4-en-1-ols when treated with sodium metal, *cis*-2-alkyl-3-chlorotetrahydrofurans give a mixture of comparable proportions of *cis*- and *trans*-alk-3-en-1-ols. *trans*-3-Chloro-2-methyltetrahydrofuran gave largely *trans*-pent-3-en-1-ol, though it was evident from both spectroscopic and chemical evidence that a little *cis*-pent-3-en-1-ol was present. Quantitative investigation of the composition of the pent-3-en-1-ols and hex-3-en-1-ols formed on ring scission of the 3-chlorotetrahydro-2-methyl- and 3-chloro-2-ethyltetrahydro-furans has now been made by an infrared spectroscopic technique described in the Experimental Section. The results are summarised in the Table. They are in agreement with our qualitative results except that the amounts of

2-Alkyl-3-chlorotetrahydrofuran	Product	
cis-2-Methyl	43% *cis*-	57% *trans*-pent-3-en-1-ol
cis-2-Ethyl	44	56 hex-3-en-1-ol
trans-2-Methyl	13	87 pent-3-en-1-ol
trans-2-Ethyl	20	80 hex-3-en-1-ol

cis-alcohol produced on fission of the *trans*-2-alkyl-3-chlorotetrahydrofurans are rather larger than we had suspected. Samples of the alcohols prepared earlier were also examined and the results agreed very well with those in the Table.

The infrared absorption spectra of *cis*- and *trans*-pairs of 2-alkyl-3-chlorotetrahydrofurans and -pyrans have been determined and in each case confirm the differing identities of the isomers. However, although it is clear that no *cis*-isomer is present in the *trans*-isomer (and *vice versa*) in the case of 3-chloro-2-methyltetrahydropyran, yet with 3-chlorotetrahydro-2-methyl- and 3-chloro-2-ethyl-tetrahydrofurans the spectra do not contain suitable bands to enable this possibilty to be excluded altogether. Were the

lower-boiling fractions azeotropes, the concentration of *cis*-isomers needed to account for the *cis*-alkenols produced on fission of the *trans*-isomers would have to be considerable.

During the present work a number of observations of preparative interest were made. For routine large-scale preparations of alkenols a technique is described in the Experimental section whereby a 2-alkyl-3-chlorotetrahydro-furan or -pyran is prepared in the usual way by using an excess of Grignard reagent, and then transferred under nitrogen slowly into a flask containing sodium under ether. This avoids isolation of the pure intermediate and the yield of *trans*-hex-4-en-1-ol has been raised from 50 to 75% overall by this procedure. It was mentioned above that 2-*tert.*-butyl-3-chlorotetrahydrofuran decomposes readily and Brandon *et al.* (*loc. cit.*) record that *tert.*-butylmagnesium bromide fails to react with 2 : 3-dibromotetrahydropyran. With 2 : 3-dichlorotetrahydropyran reaction clearly takes place but we have not succeeded in isolating a product or in subjecting it to ring fission under the above conditions. A small quantity of 2-*tert.*-butyl-3-chlorotetrahydrofuran has been isolated and with sodium gave an alcohol having the correct analysis for 5 : 5-dimethylhex-3-en-1-ol.

The feasibility of two successive chain extensions by five carbon atoms was examined by using *n*-butyl bromide and dihydropyran as starting points. These were converted into non-4-en-1-ol in the usual way. Conversion into the bromide followed by a second chain extension gave *n*-tetradeca-4 : 9-dien-1-ol, presumed to be the *trans-trans*-form from its mode of formation. The overall yield was 12% based on the first batch of dihydropyran. Ring fission becomes more sluggish as longer alkyl or alkenyl residues are employed and the yield from the second reaction was 66%, against 84% for the first. The *n*-tetradeca-4 : 9-dien-1-ol was catalytically hydrogenated to tetradecanol, and this oxidised to tetradecanoic acid to confirm its identity.

Though the 2-alkyl-3-chlorotetrahydro-furans and -pyrans are readily prepared by the methods mentioned above, the first members of the series, 3-chlorotetrahydro-furan and -pyran have hitherto been much less accessible [cf. Ou Kiun-Houo, *Ann. Chim.* (*France*), 1940, **13**, 175; Colonge and Garnier, *Bull. Soc. chim. France*, 1948, 434; Paul, *Angew. Chem.*, 1951, **63**, 301]. We now find that they are readily prepared by treatment of the 2 : 3-dichloro-compounds with lithium aluminium hydride in ether. Ring fission of the products with sodium gives but-3-en-1-ol and pent-4-en-1-ol in good yield. Pent-4-en-1-ol is more readily prepared by ring fission of tetrahydrofurfuryl chloride but this preparation of but-3-en-1-ol is convenient for small-scale work. Treatment of 2-chloromethyltetrahydropyran with sodium yields hex-5-en-1-ol in 86% yield and Eglington, Jones, and Whiting (*J.*, 1952, 2873) have shown that with sodamide it yields hex-5-yn-1-ol (80%). These authors report difficulty in the preparation of acraldehyde dimer and 2-hydroxymethyltetrahydropyran required as intermediates. Both stages proved satisfactory under the conditions used by us and higher yields of chloride were also obtained.

Eglington, Jones, and Whiting (*loc. cit.*) report that 3-chloro-2-ethyltetrahydrofuran gives only a 30% yield of hex-3-yn-1-ol when treated with sodamide. We have also obtained only poor yields of alk-3-yn-1-ols when 3-chloro-2-methyl-, -ethyl-, and -*iso*propyltetrahydrofurans are stirred with sodamide in liquid ammonia (28, 20, and 17% respectively). 3-Chlorotetrahydropyran gives a 20% yield of pent-4-yn-1-ol. In all cases low-boiling elimination products are formed and the method is of limited preparative interest.

2 : 3-Dichlorotetrahydropyran reacts with the nucleophilic reagent ethyl sodiomalonate to give 3-chloro-2-(diethoxycarbonylmethyl)tetrahydropyran, though the yield is poor and much low-boiling material is formed by solvolysis or perhaps elimination.

Experimental

Infrared absorptions were determined with a Grubb-Parsons single-beam spectrometer coupled to a Brown recorder, the pure liquids being used as capillary films.

2 : 3-*Dichlorotetrahydropyran from Tetrahydropyran.*—Dry chlorine was passed into tetrahydropyran (30 g.) in carbon tetrachloride (30 ml.) containing iodine (0·2 g.) under the conditions described for tetrahydrofuran (Part III, *J.*, 1950, 1714). Working up under similar conditions gave *trans*-2 : 3-dichlorotetrahydropyran (34 g., 63%), b. p. 86—90°/20 mm., n_D^{20} 1·4945 (Found : C, 38·7; H, 5·3; Cl, 45·65. Calc. for $C_5H_8OCl_2$: C, 38·75; H, 5·2; Cl, 45·75%). A specimen

prepared by addition of chlorine to dihydropyran (cf. Part II, *J.*, 1950, 1707) had b. p. 88—90°/20 mm., n_D^{20} 1·4946. The infrared spectra of the two compounds were identical (20 bands) in the region 700—3300 cm.$^{-1}$.

2 : 3-*Dichlorotetrahydrofuran from Dihydrofuran.*—2 : 3-Dihydrofuran (10 g.; prepared by the isomerisation method from 2 : 5-dihydrofuran) was treated in dry ether (75 ml.) with dry chlorine until a faint green tint persisted. The colour was discharged with a few drops of dihydrofuran, the ether evaporated, and the residue distilled, to give *trans*-2 : 3-dichlorotetrahydrofuran (16·1 g., 80%), b. p. 65—70°/22 mm., n_D^{20} 1·4840 (Found : Cl, 50·1. Calc. for $C_4H_6OCl_2$: Cl, 50·3%). A specimen prepared by chlorination of tetrahydrofuran (cf. Part III) had b. p. 63—66°/21 mm., n_D^{20} 1·4841. The infrared spectra of the two compounds were identical in the region 800—3300 cm.$^{-1}$.

2 : 3-Dichlorotetrahydrofuran prepared from the dihydrofuran described below had b. p. 66—72°/23 mm., n_D^{20} 1·4810 (Found : C, 34·1; H, 4·1; Cl, 49·7. Calc. for $C_4H_6OCl_2$: C, 34·1; H, 4·1%). Its infrared spectrum differed from those above only in relative intensities at 1030 and 1061 cm.$^{-1}$.

2-*Alkyl*-3-*chlorotetrahydrofurans.*—These were prepared according to the procedure of Part III, the yields of mixed isomers being methyl, 83, ethyl, 87, and *iso*propyl, 57%. Each was fractionally distilled through a 120 × 2·5-cm. glass helices-packed column with a total-reflux variable take-off. Resolution of the mixtures was not complete and the content of *cis*- and *trans*-isomers in intervening fractions was estimated refractometrically. The physical properties of the best fractions were as shown. For the methyl, ethyl, and *iso*propyl compounds the

2-Methyl, *trans* :	b. p. 130°, n_D^{19} 1·4424,	d_4^{19} 1·078,	$[R_L]_D$ 29·60
,, *cis* :	147	1·4532	1·104	29·54
2-Ethyl, *trans* :	150	1·4459	1·046	34·32
,, *cis* :	165	1·4556	1·075	34·02
2-*iso*Propyl, *trans* :	164	1·4482	1·027	38·77
,, *cis* :	178	1·4568	1·053	38·44

calculated molecular refractivities are 29·60, 34·22, and 38·84 respectively. For previous physical data on the methyl and ethyl stereoisomers see Part III. trans- (Found : C, 56·15; H, 8·6; Cl, 23·5. $C_7H_{13}OCl$ requires C, 56·55; H, 8·8; Cl, 23·85%), and cis-3-*Chlorotetrahydro*-2-*isopropylfuran* (Found : C, 56·4; H, 8·6; Cl, 23·5%) are new.

Ring Fission of the Stereoisomeric 2-*Alkyl*-3-*chlorotetrahydrofurans by Sodium.*—The *trans*-2-methyl compound gave α-pent-3-en-1-ol (64%), b. p. 136—137°, n_D^{20} 1·4342, and the *cis*-isomer gave β-pent-3-en-1-ol (70%), b. p. 137—138°, n_D^{20} 1·4357. The *trans*-2-ethyl compound gave α-hex-3-en-1-ol (59%), b. p. 63—64°/16 mm., n_D^{20} 1·4383, and the *cis*-isomer gave β-hex-3-en-1-ol (84%), b. p. 64—65°/16 mm., n_D^{20} 1·4393. The *trans*-2-*iso*propyl compound gave *α-5-methylhex-3-en-1-ol* (86%), b. p. 71—73°/15 mm., n_D^{20} 1·4372 (Found : C, 73·55; H, 12·3. $C_7H_{14}O$ requires C, 73·6; H, 12·35%), and the *cis*-isomer gave β-*5-methylhex-3-en-1-ol* (70%), b. p. 70—74°/16 mm., n_D^{20} 1·4335 (Found : C, 73·55; H, 12·4%).

For the experimental technique and comparative data on the pent-3-en-1-ols and hex-3-en-1-ols see Part III. The stereochemistry of the α- and the β-5-methylhex-3-en-1-ol has not been further investigated. They are probably mixtures of stereoisomers although the α-form gave a 1-*naphthylurethane*, m. p. 56° (Found : C, 76·2; H, 7·4; N, 4·8. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·5; N, 4·9%), and the β-form a 1-*naphthylurethane*, m. p. 63° (Found : C, 76·2; H, 7·6; N, 4·8%). Both these were crystallised from light petroleum (b. p. 60—80°).

Infrared Analysis of the Stereoisomeric Pent-3-en-1-ols and Hex-3-en-1-ols.—The pure reference compounds, *trans*-pent-3-en-1-ol and *trans*-hex-3-en-1-ol, were prepared by stereospecific reduction of the corresponding acetylenes with sodium in liquid ammonia (Part I, *J.*, 1950, 873; Sondheimer, *J.*, 1950, 878). *cis*-Pent-3-en-1-ol was a carefully fractionated specimen obtained by semihydrogenation of pent 3-yn-1-ol over palladised calcium carbonate. The infrared spectrum indicated that contamination with *trans*-isomer was very small : none could be detected chemically. Nevertheless, the figures for *cis*-content obtained in the pentenol analyses may be slightly low (1—2%) for this reason. *cis*-Hex-3-en-1-ol was a carefully purified specimen isolated from Brazilian *Mentha arvensis* oil (" leaf alcohol," cf. Parts I and IV).

For analysis, use was made of the facts that the *trans*-alcohols show strong absorption at 967 cm.$^{-1}$, which is almost non-existent in the *cis*-alcohols, whilst both show a strong band at 1040 cm.$^{-1}$ due to the hydroxyl group. The hydroxyl and the *trans*-band are of comparable intensity. This allows analysis to be carried out on liquid films without accurate control of the film thickness. The optical density of the hydroxyl band was usually about 0·4. If $a = d_{967}/d_{1040}$ for the pure *cis*-isomer, $b = d_{967}/d_{1040}$ for the pure *trans*-isomer, and $c = d_{967}/d_{1040}$

for the *cis-trans*-mixture, where d is the optical density, then % *trans*-isomer in the mixture $= 100(c - a)/(b - a)$. The validity of the method was confirmed for four mixtures of the stereoisomeric hex-3-en-1-ols (Weighed : 28, 35, 55, and 76% of *trans*-isomer. Found : 29, 35, 55, and 75% respectively) and for three mixtures of the stereoisomeric pent-3-en-1-ols (Weighed : 62, 74, and 95% of *trans*-isomer. Found : 62, 74, and 95% respectively).

Rates of Reaction of Sodium Ethoxide with cis- *and* trans-2-*Alkyl*-3-*chlorotetrahydrofurans.*—For each *cis*- and each *trans*-isomer of the 2-alkyl-3-chlorotetrahydrofurans four identical solutions were prepared and sealed in glass ampoules. These consisted of 0·1M-2-alkyl-3-chlorotetrahydrofuran in dry ethanol (10 ml.) mixed with sodium ethoxide solution (20 ml.) [made by dissolving sodium (16 g.) in dry ethanol and making the volume up to 500 ml.]. The ampoules were immersed in a water-bath at 100° for the times stated, then broken into ice-water and acidified with dilute nitric acid, and the liberated chloride ion was titrated by Volhard's method. The results are summarised in the Table.

	Reaction (%) after			
2-Alkyl-3-chlorotetrahydrofuran	20	54	84	120 min.
trans-2-Methyl	7·9	21·0	32·0	45·3
cis-2-Methyl	16·0	41·9	57·0	72·1
trans-2-Ethyl	8·9	20·6	32·6	45·5
cis-2-Ethyl	12·1	32·0	45·1	58·5
trans-2-*iso*Propyl	8·0	21·1	33·0	46·0
cis-2-*iso*Propyl	10·7	29·1	44·0	57·0

For an investigation of the products of dehydrochlorination of 2-alkyl-3-chlorotetrahydrofurans, see Normant, *Compt. rend.*, 1948, **227**, 283.

2-tert.-*Butyl*-3-*chlorotetrahydrofuran.*—A Grignard reagent was prepared from *tert.*-butyl bromide (300 g., prepared by the method of Bryce-Smith and Howlett, *J.*, 1951, 1141) and magnesium (55 g.) in ether. The reagent was cooled in ice-water, and 2 : 3-dichlorotetrahydrofuran (210 g.) added dropwise. Working up in the usual way gave crude 2-tert.-*butyl*-3-*chlorotetrahydrofuran* (153 g., 63%), b. p. 80—105°/19 mm. Attempted fractional distillation under reduced pressure caused rapid tar formation and decomposition. Six fractions were recovered from the residue by rapid distillation at 5 mm. Fraction (ii) had b. p. 61—64°/5 mm., n_D^{20} 1·4640 (Found : C, 58·9; H, 9·15; Cl, 21·0. $C_8H_{15}OCl$ requires C, 59·05; H, 9·3; Cl, 21·8%). Fraction (v) had b. p. 75—80°/5 mm., n_D^{20} 1·4652 (Found : C, 58·95; H, 9·15; Cl, 21·2%).

5 : 5-*Dimethylhex*-3-*en*-1-*ol.*—2-*tert.*-Butyl-3-chlorotetrahydrofuran (4·8 g.; mixed stereoisomers) was treated with sodium (1·5 g.) under ether (50 ml.), to give 5 : 5-*dimethylhex*-3-*en*-1-*ol* (2·3 g., 61%), b. p. 80—81°/16 mm., n_D^{20} 1·4470 (Found : C, 74·9; H, 12·4. $C_8H_{16}O$ requires C, 74·95; H, 12·6%).

trans-*Non*-4-*enyl Bromide.*—*trans*-Non-4-en-1-ol (156 g.; prepared as described in Part II) was converted by the procedure of Part III into trans-*non*-4-*enyl bromide* (139 g., 62%), b. p. 83—85°/22 mm., n_D^{20} 1·4690 (Found : C, 53·2; H, 8·45; Br, 38·7. $C_9H_{17}Br$ requires C, 52·7; H, 8·35; Br, 38·95%).

trans-trans-*Tetradeca*-4 : 9-*dien*-1-*ol.*—A Grignard reagent was prepared from magnesium (16 g., 0·66 mole) and *trans*-non-4-enyl bromide (135 g., 0·66 mole) in ether (150 ml.) and allowed to react with 2 : 3-dichlorotetrahydropyran (from dihydropyran, 0·5 mole) in the usual way. Working up gave 3-*chlorotetrahydro*-2-trans-*non*-4′-*enylpyran* (81 g., 51% calc. on the bromide), b. p. 130—150°/0·3 mm. (mixture of isomers). Ring fission of the pyran (80 g.) with sodium (17 g.) in ether (140 ml.) gave trans-trans-*tetradeca*-4 : 9-*dien*-1-*ol* (45·5 g., 66%), b. p. 139—141°/5 mm., n_D^{20} 1·4590 (Found : C, 79·35; H, 12·25. $C_{14}H_{26}O$ requires C, 79·5; H, 12·45%). The alcohol was hydrogenated over Raney nickel to myristyl alcohol, b. p. 165—168°/15 mm., m. p. 38° (Found : C, 78·3; H, 14·3. Calc. for $C_{14}H_{30}O$: C, 78·5; H, 14·1%). When oxidised with a slight excess of potassium permanganate in 20% sulphuric acid, the myristyl alcohol gave myristic acid, b. p. 121—122°/1 mm., m. p. 57° (Found : C, 73·9; H, 12·1. Calc. for $C_{14}H_{28}O_2$: C, 73·6; H, 12·4%) (lit., b. p. 122°/1 mm., m. p. 58°).

Preparation of Alk-4-*en*-1-*ols without Isolation of the* 2-*Alkyl*-3-*chlorotetrahydropyran.*—The appropriate Grignard reagent (1·2 mol.) was prepared in a three-necked round-bottomed flask (1 l.) equipped with reflux condenser, stirrer, and dropping funnel. 2 : 3-Dichlorotetrahydropyran was added in the usual way. The stirrer and reflux condenser were then transferred to a second similar flask, containing powdered sodium (2 g.-atoms) under ether, and replaced by a rubber bung and a connection to a nitrogen cylinder. In place of the dropping

funnel a glass bridge (8 mm. bore) equipped with rubber bungs was inserted so that it reached the bottom of the flask. The other end was inserted in the flask containing the sodium so that it was well above the surface of the ether. By adjustment of the nitrogen pressure the contents of the first flask were delivered dropwise into the second (4—5 hr.) and any remaining material was washed in with a little ether. Care must be taken in starting the sodium ring fission as initiation seems to be retarded by the excess of Grignard reagent. The product was worked up in the usual manner.

3-Chlorotetrahydropyran.—2 : 3-Dichlorotetrahydropyran (160 g.) in anhydrous ether (350 ml.) was treated with a suspension of lithium aluminium hydride (10 g.) in ether (400 ml.) so that gentle refluxing was maintained, then heated under reflux for 40 min. The excess of reagent was decomposed with wet ether and then dilute sulphuric acid. The ethereal layer was dried, the solvent removed under a column, and the residue distilled. The fraction, b. p. 137—146°, was collected (70 g., 56%; n_D^{20} 1·4626), and when redistilled *3-chlorotetrahydropyran* had b. p. 52—54°/13 mm., n_D^{20} 1·4620 (Found : C, 50·0; H, 7·6; Cl, 30·0. C_5H_9OCl requires C, 49·8; H, 7·5; Cl, 29·4%). An experiment on one-tenth of the above scale gave a yield of 73% (b. p. 140—143°, n_D^{15} 1·4652).

3-Chlorotetrahydrofuran.—2 : 3-Dichlorotetrahydrofuran (30 g.) in ether (70 ml.) was treated with lithium aluminium hydride (2 g.) in ether as described above. *3-Chlorotetrahydrofuran* (15 g., 67%), b. p. 59—61°/30 mm., n_D^{20} 1·4532, was isolated (Found : C, 45·1; H, 6·55; Cl, 33·3. Calc. for C_4H_7OCl : C, 45·05; H, 6·6; Cl, 33·25%).

Pent-4-en-1-ol.—3-Chlorotetrahydropyran (8·5 g.) in ether (30 ml.) was added slowly to sodium (4 g.) under dry ether (15 ml.). Working up gave pent-4-en-1-ol (4·4 g., 73%), b. p. 134—137°, n_D^{20} 1·4301. The 1-naphthylurethane had m. p. 62°. Robinson and Smith (*J.*, 1936, 195) give b. p. 135—137°, n_D^{20} 1·4312. For the 1-naphthylurethane, Schniepp and Geller (*J. Amer. Chem. Soc.*, 1945, **67**, 54) give m. p. 61·5—62°.

But-3-en-1-ol.—3-Chlorotetrahydrofuran (10 g.) was added dropwise to sodium (5 g.) under ether (10 ml.), the volume being made up to 50 ml. when reaction had started. But-3-en-1-ol (5·4 g., 79%) had b. p. 111—114°, n_D^{20} 1·4218. Its 1-naphthylurethane, crystallised from light petroleum (b. p. 60—80°), had m. p. 77° (Found : C, 74·5; H, 6·2. Calc. for $C_{15}H_{15}O_2N$: C, 74·7; H, 6·3%). Birch and McAllan (*J.*, 1951, 2556) give b. p. 113·5°/760 mm., n_D^{20} 1·4200. Roberts and Mazur (*J. Amer. Chem. Soc.*, 1951, **73**, 2509) give m. p. 75·2—75·6° for the 1-naphthylurethane.

Reaction of 3-Chlorotetrahydro-furans and -pyrans with Sodamide and Liquid Ammonia.—Typical conditions were as follows : Sodamide was prepared in liquid ammonia (500 ml.) from sodium (26 g.) in the presence of ferric nitrate. 3-Chlorotetrahydropyran (34·4 g.) was added dropwise with vigorous stirring which was continued for 6 hr. and then overnight in the presence of anhydrous ether (200 ml.). Next day ammonia solution (*d* 0·88) was added and the ethereal layer separated. The aqueous phase was extracted with ether, and the ethereal extracts were united, dried (Na_2SO_4), and distilled. Two main fractions were obtained : (i) b. p. 85—88°, n_D^{20} 1·4406 (12·4 g., 52%) (Found : C, 71·0; H, 9·4. Calc. for C_5H_8O : C, 71·4; H, 9·6%) (lit. for dihydropyran, b. p. 85°, n_D^{20} 1·4405); (ii) b. p. 150—155°, n_D^{20} 1·4488 (4·9 g., 20%). The 1-naphthylurethane from fraction (ii) had m. p. 83° (Found : C, 75·75; H, 5·85. Calc. for $C_{16}H_{15}O_2N$: C, 75·9; H, 5·95%), undepressed by the authentic 1-naphthylurethane of pent-4-yn-1-ol. Paul and Tchelitcheff (*Compt. rend.*, 1950, **230**, 1473) give b. p. 154—155°, n_D^{19} 1·4432, for pent-4-yn-1-ol. The intermediate fraction (1·1 g.) appeared, from the refractive index (n_D^{20} 1·4638), to contain unchanged 3-chlorotetrahydropyran.

Under similar conditions 3-chlorotetrahydro-2-methylfuran gave pent-3-yn-1-ol (b. p. 153—160°; 28%); the 1-naphthylurethane, m. p. 119°, was undepressed by authentic material (m. p. 119°). The low-boiling fraction (b. p. 78—85°; 32%) was 2 : 3-dihydro-5-methylfuran (Found : C, 71·2; H, 9·5. Calc. for C_5H_8O : C, 71·4; H, 9·6%).

3-Chloro-2-ethyltetrahydrofuran gave 5-ethyl-2 : 3-dihydrofuran (34%), b. p. 100—110° (Found : C, 73·2; H, 10·3. Calc. for $C_6H_{10}O$: C, 73·4; H, 10·3%), and hex-3-yn-1-ol (20%), b. p. 164—166°. The 1-naphthylurethane of the latter had m. p. 85° (Sondheimer, *loc. cit.*, gives m. p. 84—85°).

3-Chlorotetrahydro-2-*iso*propylfuran gave 2 : 3-dihydro-5-*iso*propylfuran (37%), b. p. 120—127° (Found : C, 74·2; H, 10·7. Calc. for $C_7H_{12}O$: C, 74·95; H, 10·8%), and 5-methylhex-3-yn-1-ol (17%), b. p. 160—163°, which formed a *1-naphthylurethane*, m. p. 88° (Found : C, 76·7; H, 6·7. $C_{18}H_{19}O_2N$ requires C, 76·9; H, 6·8%).

When 2 : 3-dihydro-5-methylfuran, 2 : 3-dihydrofuran, and 3 : 4-dihydropyran were stirred with sodamide in liquid ammonia, no acetylenic alcohol was formed.

2-Formyl-3 : 4-dihydropyran.—Redistilled 96% acraldehyde (295 g.), benzene (350 ml.), and quinol (4 g.) were placed in a stainless-steel autoclave (1 l.) fitted with a magnetically operated stirrer. The temperature was raised rapidly to 160° and kept just above this figure for 4 hr. The product was distilled through a 30-cm. Dufton column to give, after removal of the benzene and acraldehyde, 2-formyl-3 : 4-dihydropyran (108 g., 37%), b. p. 52—53°/17 mm., n_D^{20} 1·4646. FIAT Final Report 1157, p. 13, gives b. p. 49°/14 mm., n_D^{20} 1·4660. There were 53 g. of resinous residue.

Tetrahydro-2-hydroxymethylpyran.—Formyldihydropyran (149 g.) was hydrogenated (4 hr.) at 60°/30 atm. in ethanol (88 g.) and benzene (88 g.) with Raney nickel catalyst (21 g.). Distillation gave tetrahydro-2-hydroxymethylpyran (126 g., 81%), b. p. 182—190°, n_D^{20} 1·4566. On redistillation this had b. p. 180—183°/760 mm., n_D^{20} 1·4566 (Found: C, 61·9; H, 10·4. Calc. for $C_6H_{12}O_2$: C, 62·0; H, 10·3%). B.P. 595,379 gives b. p. 184—186°/760 mm., $n_D^{24\cdot5}$ 1·4565.

2-Chloromethyltetrahydropyran.—For our preferred procedure, see Crombie, Harper, Newman, Thompson, and Smith (preceding paper).

Di(tetrahydropyran-2-ylmethyl) sulphite was obtained by adding thionyl chloride (19 ml.) to tetrahydro-2-hydroxymethylpyran (58 g.) in pyridine (44 g.) below 25°. Stirring (3 hr.), extraction with ether (7 × 30 ml.), washing with water, drying, and distillation gave the sulphite, b. p. 135—137°/0·07 mm., n_D^{20} 1·4833 (Found: C, 51·8; H, 7·9; S, 10·4. $C_{12}H_{22}O_5S$ requires C, 51·8; H, 7·9; S, 11·5%).

Hex-5-en-1-ol.—Ring fission of 2-chloromethyltetrahydropyran (16·8 g.) with sodium (6 g.) in the usual way gave hex-5-en-1-ol (10·8 g., 86%), b. p. 152—155°, n_D^{20} 1·4348 (Found: C, 71·7; H, 12·0. $C_6H_{12}O$ requires C, 72·0; H, 12·0%). The 1-naphthylurethane had m. p. 62°.

3-Chloro-2-(diethoxycarbonylmethyl)tetrahydropyran.—Sodium (5·95 g.) was dissolved in anhydrous ethanol (150 ml.), and ethyl malonate (41·5 g.) added. After stirring (20 min.), 2 : 3-dichlorotetrahydropyran (31 g.) was added during 1 hr. and stirring continued (30 min.). After refluxing (30 min.), part of the solvent was removed under reduced pressure and water added. The product was thoroughly extracted with ether, the solvent evaporated, and the residue distilled. After elimination of low-boiling material a fraction, b. p. >70°/0·3 mm., n_D^{15} 1·4575 (7·4 g.), was obtained. When purified by two further distillations the *diester* (3·0 g.) had b. p. 110—115°/0·08 mm., n_D^{15} 1·4642 (Found: C, 51·9; H, 6·7; Cl, 12·9. $C_{12}H_{19}O_5Cl$ requires C, 51·7; H, 6·85; Cl, 12·7%).

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27. *Sesquiterpenoids. Part VII.* The Constitution of Tenulin, a Novel Sesquiterpenoid Lactone.*

By D. H. R. BARTON and P. DE MAYO.

The sesquiterpenoid lactone tenulin has been shown to contain a masked acetyl grouping which rearranges very easily to a true acetate residue in the derived *iso*tenulin. Inter-relation of the functional groups of tenulin has been effected. Dehydrogenation of suitable derivatives has afforded chamazulene and linderazulene. Based on these and earlier observations, constitutions have been deduced for tenulin and *iso*tenulin, and their derivatives.

THE crystalline bitter principle tenulin, $C_{17}H_{22}O_5$, was isolated by Clark (*J. Amer. Chem. Soc.*, 1939, **61**, 1836; 1940, **62**, 597) from various *Helenium* species (*H. tenuifolium*, *H. elegans*, *H. badium*, and *H. montanum*). The compound has interesting physiological properties and was studied in some detail by this author (*locc. cit.*; also *ibid.*, 1940, **62**, 2154) and later by Ungnade *et al.* (Ungnade and Hendley, *ibid.*, 1948, **70**, 3921; Ungnade, Hendley, and Dunkel, *ibid.*, 1950, **72**, 3818). The more important features of Clark's

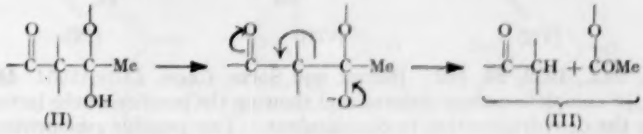
* Part VI, *J.*, 1954, 4665.

work can be summarised as follows. Tenulin is isomerised by mild alkali to *iso*tenulin. Both compounds are smoothly hydrogenated to dihydro-derivatives, both of which afford phenylhydrazones. Both compounds give dibromides which easily evolve one mol. of hydrogen bromide. Pyrolysis of tenulin affords, first, anhydrotenulin, $C_{17}H_{20}O_4$, and then pyrotenulin, formulated as $C_{13}H_{16}O_3$. Treatment of *iso*tenulin with sulphuric acid gave deacetyl*iso*tenulin (from which *iso*tenulin was regenerated by acetylation) and one mol. of acetic acid. Similar hydrolysis of dihydro*iso*tenulin with either acid or alkali gave comparable results. Oxidation of tenulin or *iso*tenulin with alkaline hydrogen peroxide gave tenulinic acid, $C_{15}H_{20}O_7$, characterised as its methyl ester. Acetylation of the acid afforded acetyltenulinic acid, $C_{17}H_{22}O_8$, which was the direct product of the oxidation of tenulin or *iso*tenulin with potassium permanganate. On the basis of these experiments Clark concluded that the functional groups of tenulin could be symbolised as in (I).

$$C_{15}H_{18}O\begin{cases}\text{-OH}\\ \\ =O\\ O\text{·COMe}\end{cases}$$
(I)

Ungnade and his collaborators (*locc. cit.*) reported that the ultraviolet absorption spectra of tenulin and *iso*tenulin showed them to be αβ-unsaturated ketones. All compounds were regarded as lactones on the basis of their infrared spectra and it was shown specifically that *iso*tenulin consumed two mols. of alkali, one for hydrolysis of an acetate residue (see above) and the other for the opening of a lactone ring. Now if Clark's partial symbol (I) be accepted, there is insufficient uncharacterised oxygen left for the formation of a lactone ring. It was this paradox which first attracted us to the chemistry of tenulin. Our own analysis of the problem is presented in the sequel.

Extraction of *H. tenuifolium* afforded, without difficulty, tenulin. This showed $\lambda_{max.}$ 226 mμ (ε 7000) and gave bands in the infrared as follows: (*a*) (in $CHCl_3$) 1772 (γ-lactone), 1708 and 1595 (*cyclo*pentenone), and 3620 (hydroxyl); (*b*) (in Nujol) 1778 (γ-lactone), 1695 and 1590 (*cyclo*pentenone), and 3450 cm.$^{-1}$ (hydroxyl). The position of the ultraviolet absorption maximum of tenulin [accepted as a *cyclo*pentenone (see above)] indicates only two substituents on the double bond (Woodward, *ibid.*, 1941, **63**, 1123; 1942, **64**, 76; Gillam and West, *J.*, 1942, 486). A choice between the arrangements (*A*) O:Ċ·CH:C< and (*B*) O:Ċ·Ċ:CH· was made by ozonolysis. Under neutral conditions this afforded formic acid indicative, unless some extra complication is introduced, of grouping (*A*), not (*B*). On brief treatment with boiling (London) tap-water tenulin was smoothly isomerised to *iso*tenulin. This showed $\lambda_{max.}$ 226 mμ (ε 7400) and gave infrared bands in Nujol at 1778 (γ-lactone), 1705 and 1588 (*cyclo*pentenone), 1748 and 1238 cm.$^{-1}$ (acetate). Clearly *iso*tenulin has the same *cyclo*pentenone system as tenulin; this was confirmed by ozonolysis which also gave formic acid. The most interesting aspect of these results is that tenulin contains no acetate grouping, but does possess a hydroxyl group, whereas the converse holds for *iso*tenulin.* In agreement, tenulin gave no acetic acid on acid hydrolysis, but 1 mol. of this acid if treated first with alkali. Also *iso*tenulin gave 1 mol. of acetic acid under acid conditions according to the usual method of determination. The simplest explanation for these remarkable facts is that tenulin contains the masked acetyl system (II), cleavage of which by base would afford *iso*tenulin (III).

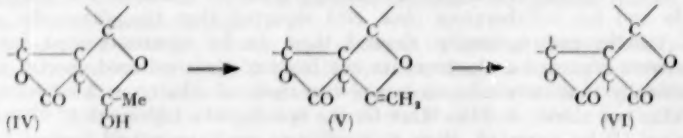


(II) (III)

The carbonyl group which triggers this rearrangement could be either the ketone of the *cyclo*pentenone or the carbonyl of the lactone grouping. A distinction was made as follows. Dihydrotenulin, which showed the expected bands (in $CHCl_3$) at 1770 (γ-lactone), 1738

* When investigating the conversion of tenulin into *iso*tenulin we studied, first, one of Clark's methods, *viz.*, trituration with 5% aqueous sodium carbonate. To test if an enolic intermediate was formed [as is indeed the case; see scheme (II) ⟶ (III)] deuterium oxide was used. Although a product of the correct m. p. resulted it contained no deuterium. The enigma was resolved when it was found that the product was impure tenulin (isolated by chromatography). This particular method for making *iso*tenulin is not therefore reliable.

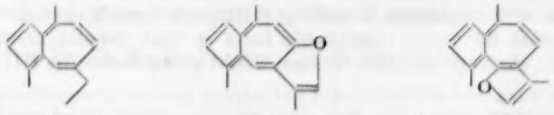
(*cyclo*pentanone), and **3500** cm.$^{-1}$ (hydroxyl), was smoothly rearranged to dihydro*iso*tenulin; the masked acetate grouping, therefore, cannot be attached vinylogously β with respect to the ketone group. Further, dihydrotenulin oxime also rearranged smoothly to dihydro*iso*tenulin oxime; hence ketonic carbonyl does not induce the rearrangement and the masked acetate grouping must, by exclusion, be attached β to the lactone-carbonyl group, as in (IV). This was confirmed in the following way. Pyrotenulin, which Clark had formulated as $C_{13}H_{16}O_3$ (see above), consumes only 1 mol. of alkali (Ungnade, Hendley, and Durkel, *loc. cit.*) and shows only end-absorption in the ultraviolet region. We have shown that pyrotenulin is identical with a compound obtained by Clark by the action of acetic anhydride–sodium acetate on tenulin. Clark tentatively formulated this compound as $C_{22}H_{26}O_5$ but noted that it contained no acetate residue. The correct formula for pyrotenulin is $C_{17}H_{20}O_4$ with the partial formulation as in (V).



(IV) (V) (VI)

In the infrared spectrum pyrotenulin showed the following bands : (*a*) (in $CHCl_3$) **1778** (γ-lactone), **1754** (*cyclo*pentanone), **1656** and **1605** (C:C of vinyl ether); (*b*) (in Nujol) **1772** (γ-lactone), **1752** (*cyclo*pentanone), **1673**, **1630**, and **810** cm.$^{-1}$ (·O·Ċ:CH$_2$) (see Meakins, *J.*, 1953, 4170). Treatment of dihydrotenulin with acetic anhydride–sodium acetate gave anhydrodihydrotenulin, $C_{17}H_{22}O_4$ [as (V)], which on ozonolysis afforded formaldehyde and the expected bis-γ-lactone (VI). Anhydrodihydrotenulin showed bands (in $CHCl_3$) at **1784** (γ-lactone), **1738** (*cyclo*pentanone), and **1670** and **1652** cm.$^{-1}$ (C:C of vinyl ether). The bis γ-lactone gave bands (in $CHCl_3$) at **1800** and **1765** (γ-lactones attached to the same carbon atom; cf. Fox and Martin, *Proc. Roy. Soc.*, **1938**, *A*, **167**, 257; Bergmann and Pinchas, *Rec. Trav. chim.*, 1952, **71**, 161) and at 1740 cm.$^{-1}$ (*cyclo*pentanone).

We shall next abbreviate further discussion by deducing complete structures for tenulin and *iso*tenulin and show how these explain all significant prior knowledge. Reduction of *iso*tenulin with potassium borohydride and dehydrogenation of the product gave chamazulene (VII) (Meisels and Weizmann, *J. Amer. Chem. Soc.*, 1953, **75**, 3865; Šorm, Herout, and Takeda, *Chem. Listy*, 1954, **48**, 281; Novak, Šorm, and Sicher, *ibid.*, p. 1648). This establishes the position of fourteen of the fifteen carbon atoms of the basic skeleton. Reduction of dihydro*iso*tenulin with lithium aluminium hydride and dehydrogenation of the product gave linderazulene (VIII) [not (IX)] [Takeda and Nagata, *Pharm. Bull.* (*Japan*) 1953, **1**, 164; cf. Takeda and Shimada, *J. Pharm. Soc. Japan*, 1944, **64**, 32; Kondo



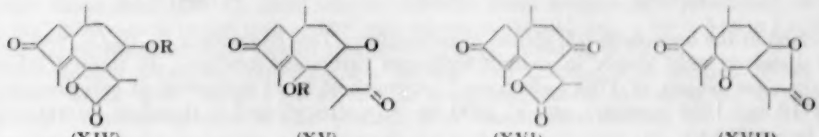
(VII) (VIII) (IX)

and Takeda, *ibid.*, 1939, **59**, 162; Herout and Šorm, *Chem. Listy*, 1954, **48**, 706], thus establishing the complete carbon skeleton and showing the position of the lactonic carbonyl group lost in the dehydrogenation to chamazulene. Two possible *cyclo*pentenone formul-

(X) (XI) (XII) (XIII)

ations must be considered, (X) and (XI). The correctness of the former was shown as follows. Treatment of tenulin with aqueous sodium hydrogen carbonate gave, besides

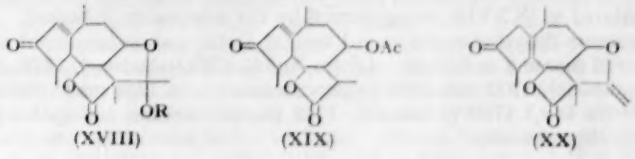
the known deacetyl*iso*tenulin (see above), a new conjugated ketone which we designate deacetyl*neo*tenulin. This showed $\lambda_{max.}$ 240 mμ (ε 16,000) and gave infrared bands (in Nujol) at 1765 (γ-lactone), 1682 and 1628 (*cyclo*pentenone), and at 3300 cm.$^{-1}$ (hydroxyl) and furnished *neo*tenulin on acetylation. These compounds must be represented by either (XII), based on (X), or (XIII), based on (XI). That (XII) was correct was shown by ozonolysis of deacetyl*neo*tenulin which afforded, under neutral conditions, acetic acid. Deacetyl*neo*tenulin must therefore be represented by either (XIV or XV; R = H).* Chromic acid oxidation gave deacetyldehydro*neo*tenulin, (XVI) or (XVII). This showed $\lambda_{max.}$ 245 mμ (ε 12,000) and had infrared bands as follows: (*a*) (in $CHCl_3$) 1785 (γ-lactone), 1708 and 1635 (*cyclo*pentenone), and 1730 cm.$^{-1}$ (somewhat displaced *cyclo*heptanone);



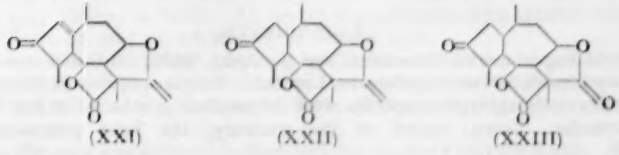
(XIV) (XV) (XVI) (XVII)

(*b*) (in Nujol) 1768 (γ-lactone), 1698 and 1628 (*cyclo*pentenone), and 1730 cm.$^{-1}$ (somewhat displaced *cyclo*heptanone). The data are not consistent with the ene-1 : 4-dione structure (XVII), which would have shown an infrared band between 1690 and 1670 cm.$^{-1}$ as well as the usual *cyclo*pentenone bands. Also the shape of the ultraviolet absorption curve was quite different (see Experimental section) from that of cholest-4-ene-3 : 6-dione. Dehydrodeacetyl*neo*tenulin was not reducible by zinc and acetic acid, as would have been expected if the ene-1 : 4-dione structure (XVII) were correct. The position of the *cyclo*heptanone infrared band in the compounds mentioned above is somewhat displaced (expected position about 1700 cm.$^{-1}$). This feature is common to all the corresponding ketonic derivatives of tenulin that we have examined. For example, oxidation of deacetyl-*iso*tenulin afforded deacetyldehydro*iso*tenulin. This showed infrared maxima (in $CHCl_3$) at 1780 (γ-lactone), 1738 (displaced *cyclo*heptanone), and 1692 and 1596 cm.$^{-1}$ (*cyclo*-pentenone).

In summary, on the basis of all this evidence, tenulin is formulated as (XVIII; R = H), *iso*tenulin as (XIX), pyrotenulin as (XX) (or an equivalent βγ-unsaturated structure), anhydrotenulin as (XXI), anhydrodihydrotenulin as (XXII), the derived bis-γ-lactone as (XXIII), and *neo*tenulin as (XIV; R = Ac).



(XVIII) (XIX) (XX)

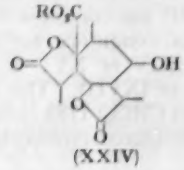


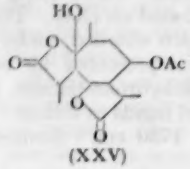
(XXI) (XXII) (XXIII)

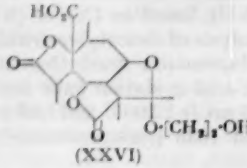
Tenulinic acid is readily formulated as (XXIV; R = H). In agreement the methyl ester (XXIV; R = Me) showed infrared bands in $CHCl_3$ at 1774 (γ-lactones and ester; broad unsymmetrical band, strength indicative of three carbonyl groups), and 3600 cm.$^{-1}$

* In principle the position of the lactone ring could be different in deacetyl*neo*tenulin from that in tenulin. However deacetyl*neo*tenulin can be obtained from the sodium hydrogen carbonate solution *without* acidification; hence the lactone ring is not opened in the transformation and thus has no opportunity to close in the alternative direction. Even if the lactone ring had opened, the work on tenulinic acid discussed in the text shows that it would close back again to its original position.

(hydroxyl). Oxidation of the methyl ester afforded methyl dehydrotenulinate which gave infrared maxima in $CHCl_3$ at 1800 (γ-lactones), 1760 (somewhat displaced methoxycarbonyl), and 1722 cm.$^{-1}$ (*cyclo*heptanone; cf. above). An analogue of tenulinic acid was

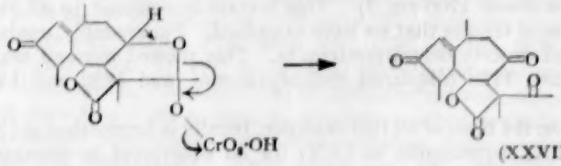

(XXIV)


(XXV)


(XXVI)

obtained in the ozonolysis (cf. above) of *iso*tenulin. This compound, $C_{16}H_{22}O_7$, was acidic but dissolved only slowly in sodium hydrogen carbonate solution. It showed infrared maxima (in Nujol) at 1764 (γ-lactones; strength of band indicative of two groupings), at 1712 and 1255 (acetate), and at 3400 cm.$^{-1}$ (hydroxyl) and is therefore formulated as the lactol (XXV).

In his last paper on tenulin Clark (*loc. cit.*) noted that it reacted very easily with ethylene glycol to furnish an acylable compound, $C_{19}H_{32}O_6$, readily cleaved by acid treatment to regnerate its precursors. This would be an expected reaction for our hemiketal tenulin structure; the ether may be formulated as (XVIII; R = $[CH_2]_2$·OH). Oxidation of the ether with *either* potassium permanganate *or* alkaline hydrogen peroxide afforded the *same* acid, $C_{19}H_{26}O_9$. This acid may be formulated as (XXVI); the failure to lose the acetic acid generating residue (see Clark, *loc. cit.*) under alkaline conditions (contrast tenulinic acid) is unexceptional.


(XXVII)

An interesting observation incidental to our work is that, whilst *iso*tenulin is stable to chromic acid at room temperature, tenulin itself is easily oxidised to dehydrotenulin. This is formulated as (XXVII), being formed by the mechanism indicated. In agreement with this structure dehydrotenulin gave 1 mol. of acetic acid on treatment with alkali and showed infrared maxima as follows: (*a*) (in Nujol) 1760 (γ-lactone), 1728 (methyl ketone and *cyclo*heptanone), 1700 and 1590 (*cyclo*pentenone), and 1354 cm.$^{-1}$ (methyl of methyl ketone); (*b*) (in CCl_4) 1780 (γ-lactone), 1742 (methyl ketone and *cyclo*heptanone), and 1710 cm.$^{-1}$ (*cyclo*pentenone).

Experimental

For general experimental directions, see *J.*, 1952, 2339. Infrared spectra were kindly determined by Messrs. Glaxo Laboratories Limited. Unless specified to the contrary, $[\alpha]_D$ are in $CHCl_3$; ultraviolet absorption spectra were determined in ethanol on the Unicam S.P. 500 Spectrophotometer. Unless stated to the contrary, the light petroleum used was of b. p. 40—60°.

Tenulin.—This compound was isolated by Ungnade and Hendley's method (*J. Amer. Chem. Soc.*, 1948, **70**, 3921). Recrystallised from benzene, tenulin had m. p. about 130—140° with evolution of benzene (isolated and identified spectroscopically). The partial melt rapidly resolidified and the final m. p. depended on the rate of heating and the original form of the tenulin crystals. Tenulin was obtained in at least three different crystalline forms: solvated square heavy plates (from hot benzene), solvated small prisms [from hot benzene–light petroleum (b. p. 60—80°)] and needles (from the same solvent mixture in the cold). The needles are unsolvated and rapidly change in contact with solvent into the small prisms. The m. p. of

tenulin, which may be as high as 215°, is indefinite. In contrast, the rotation of all specimens was the same: $[\alpha]_D$ −20° (*c* 2·18 in EtOH), −21° (*c* 1·99 in EtOH), −22° (*c* 1·86 in EtOH), −21° (*c* 1·46), −24° (*c* 0·88). $\lambda_{max.}$ was at 226 mμ (ε 7000). Tenulin was recovered unchanged after treatment with pyridine–acetic anhydride overnight at room temperature.

Acetyl determinations. (*a*) Acetyl determination in the usual way with 30% sulphuric acid (H. Roth, "Pregl's Quantitative Organic Microanalysis," J. and A. Churchill Ltd., London, 1937) gave no volatile acid. (*b*) Hydrolysis by concentrated sulphuric acid at 90° for 3 min., followed by dilution, partial neutralisation, and distillation, afforded 0·3 mol. of volatile acid. (*c*) Hydrolysis with 5N-sodium hydroxide in the usual way (*op. cit.*, p. 197) gave 1·0 mol. of volatile acid.

Trituration of tenulin with 5% aqueous (protium or deuterium) sodium carbonate (Clark, *J. Amer. Chem. Soc.*, 1939, **61**, 1836) afforded material (from benzene–light petroleum), m. p. 160—161° (preliminary partial melt at 130° with solvent evolution), $[\alpha]_D$ −24° (*c* 0·98 in EtOH). Chromatography over silica gel yielded only tenulin (m. p., mixed m. p., $[\alpha]_D$).

Dehydrotenulin.—Tenulin (240 mg.) was treated with chromic acid solution (0·05N in "AnalaR" acetic acid; 50 ml.) for 40 min. at room temperature (0·8 atom of "oxygen" consumed). Chromatography of the product over deactivated neutral alumina (10 g.) (13 fractions) gave *dehydrotenulin*, 4 fractions eluted with benzene–ether (19 : 1) (50 mg.), m. p. (prisms from benzene) 203—205° (effervescence), $[\alpha]_D$ −83° (*c* 1·10), −81° (*c* 0·97), −82° (*c* 0·94) in EtOH, $\lambda_{max.}$ 226 mμ (ε 7500) (Found: C, 66·95; H, 6·55. $C_{17}H_{20}O_5$ requires C, 67·1; H, 6·6%). Acetyl determination by the alkaline method (see above) gave 0·88 mol. of volatile acid. From the same chromatogram elution with benzene–ether (7 : 3) (four fractions) gave unchanged tenulin (85 mg.). Increased uptake of chromic acid did not increase the yield of dehydrotenulin.

Pyrotenulin.—(*a*) (cf. Clark, *ibid.*, 1940, **62**, 597) Tenulin (250 mg.) was heated under nitrogen to 200°. After the evolution of benzene had ceased, the flask was removed, the bath heated to 300°, and the flask again heated at this temperature until a further evolution of gas had ceased (10 min.). The product was chromatographed over neutral deactivated alumina. Elution with benzene–light petroleum (7 : 3) gave pyrotenulin, m. p. (from methanol) 235—237°, $[\alpha]_D$ −34° (*c* 1·10), ε 6400 at 205 mμ, ε 5200 at 210 mμ, ε 2100 at 220 mμ [Clark (*loc. cit.*) gives m. p. 235—236°, but Ungnade, Hendley, and Dunkel (*ibid.*, 1950, **72**, 3818) record m. p. 209°].

(*b*) (cf. Clark, *ibid.*, 1939, **61**, 1836) Tenulin (100 mg.) was refluxed in acetic anhydride (1 ml.) containing sodium acetate (25 mg.) for 50 min. The acetic anhydride was removed *in vacuo* and the product, worked up in the usual way, was crystallised to give pyrotenulin, m. p. (from methanol) 233—235°, $[\alpha]_D$ −31° (*c* 0·60). According to Clark (*loc. cit.*) this procedure affords a compound, $C_{32}H_{36}O_5$, m. p. 240°. The identity of the compounds prepared under (*a*) and (*b*) was confirmed by mixed m. p. and infrared spectra (in $CHCl_3$).

Dihydrotenulin.—This compound, prepared by Clark's method (*loc. cit.*), had m. p. 184—186° (Clark gives m. p. 182° and 172°), $[\alpha]_D$ +86° (*c* 1·38), +76° (*c* 1·24 in EtOH), +76° (*c* 1·31 in EtOH). Treatment with pyridine–hydroxylamine hydrochloride overnight at room temperature afforded *dihydrotenulin oxime*, m. p. (from chloroform–benzene) 210—211°, $[\alpha]_D$ +54° (*c* 1·38), +54° (*c* 1·02) (Found: N, 4·05. $C_{17}H_{25}O_5N$ requires N, 4·35%).

iso*Tenulin* (cf. Ungnade and Hendley, *loc. cit.*).—Tenulin (600 mg.) was added to boiling (London) tap-water and the solution boiled for 2 min. Cooling furnished *iso*tenulin (370 mg.) as long needles, m. p. 160—161°, $[\alpha]_D$ +6° (*c* 1·57), +4° (*c* 1·44), +9° (*c* 1·14 in EtOH), +8° (*c* 0·83 in EtOH), $\lambda_{max.}$ 226 mμ (ε 7400). An acetyl determination with diluted sulphuric acid in the usual way (Roth, *op. cit.*) gave 0·96 mol. of volatile acid.

Dihydroisotenulin.—This compound, prepared by Clark's method (*loc. cit.*), had m. p. 148—149°, $[\alpha]_D$ +111° (*c* 1·80). It gave an *oxime*, m. p. (from ethyl acetate–light petroleum) 174—175·5°, $[\alpha]_D$ +109° (*c* 1·63) (Found: C, 63·4; H, 7·35; N, 3·85. $C_{17}H_{25}O_5N$ requires C, 63·15; H, 7·8; N, 4·35%).

Dihydrotenulin (30 mg.) was refluxed in (London) tap-water (3 ml.) for 2 min. Cooling and crystallisation from ether–light petroleum afforded dihydro*iso*tenulin, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +114° (*c* 0·83)}.

Similarly dihydrotenulin oxime (30 mg.) was treated as above. Cooling and crystallisation from ethyl acetate–light petroleum afforded dihydro*iso*tenulin oxime, identified by m. p., mixed m. p. and rotation {$[\alpha]_D$ +109° (*c* 0·97)}.

Ozonolysis of iso*Tenulin.*—(a) *iso*Tenulin (290 mg.) in chloroform (25 ml.) was ozonised at 0° for 45 min. (disappearance of ultraviolet maximum). Water (15 ml.) was added and the chloroform evaporated. The product was again taken up in chloroform. Extraction with

sodium hydrogen carbonate solution afforded the lactol (XXV), m. p. (from aqueous methanol) 233—236°, $[\alpha]_D$ +64° (*c* 1·00) (Found : C, 59·2; H, 6·75. $C_{16}H_{22}O_7$ requires C, 58·9; H, 6·8%). The compound dissolved only slowly in aqueous sodium hydrogen carbonate.

(b) *iso*Tenulin (100 mg.) in carbon tetrachloride (10 ml.) was ozonised at 0° until the ultraviolet absorption maximum had disappeared. Water (10 ml.) was added and the mixture distilled. The total distillate was neutralised with aqueous sodium hydroxide, and the aqueous layer treated with ethanolic *p*-bromophenacyl bromide in the usual way. Chromatography of the product over alumina gave *p*-bromophenacyl formate (8 mg.), identified by m. p. and mixed m. p. Ozonolysis of tenulin under the same conditions yielded a similar result.

Anhydrodihydrotenulin.—Dihydrotenulin (250 mg.) in acetic anhydride (30 ml.) containing sodium acetate (250 mg.) was refluxed for 7 hr. The acetic anhydride was removed *in vacuo* and the product worked up in the usual way. Chromatography over neutral deactivated alumina (8 g.) and elution with benzene gave *anhydrodihydrotenulin*, m. p. [from benzene–light petroleum (b. p. 60—80°)] 173—175°, $[\alpha]_D$ +55° (*c* 1·50) (Found : C, 70·05; H, 7·7. $C_{17}H_{22}O_4$ requires C, 70·3; H, 7·65%). This compound gave a strongly positive tetranitromethane test.

Ozonolysis of Anhydrodihydrotenulin.—Anhydrodihydrotenulin (130 mg.) in chloroform (5 ml.) was ozonised at 0° until the solution gave no colour with tetranitromethane (10 min.). Water (10 ml.) was added and the chloroform and water were distilled off. The crystalline residue readily gave the *dilactone* (XXIII), m. p. (from methanol) 256—258°, $[\alpha]_D$ +82° (*c* 1·49) (Found : C, 65·65; H, 6·9. $C_{14}H_{20}O_6$ requires C, 65·75; H, 6·9%). To the combined distillate was added dimedone (100 mg.) in methanol (5 ml.). The chloroform and most of the methanol were removed on the steam-bath, whereupon the dimedone–formaldehyde derivative crystallised (6 mg.; identified by m. p. and mixed m. p.).

Tenulinic Acid and its Derivatives.—Tenulinic acid was prepared with alkaline hydrogen peroxide according to Clark (*J. Amer. Chem. Soc.*, 1940, **62**, 597) and converted into the methyl ester {m. p. 206—208°, $[\alpha]_D$ +81° (*c* 1·00)} with diazomethane.

Methyl tenulinate (333 mg.) was treated with chromic acid in " AnalaR " acetic acid (25 ml.; 0·12N) at room temperature. After 1½ hr. the uptake of chromic acid had reached 1·0 atom of " oxygen " and was unchanged later. Working up in the usual way gave *methyl dehydrotenulinate*, m. p. (from benzene–light petroleum) 228—229°, $[\alpha]_D$ −9° (*c* 2·04) (Found : C, 58·6; H, 6·6. $C_{14}H_{20}O_7$ requires C, 59·25; H, 6·2%; several samples of this compound, after repeated crystallisation, were analysed by different analysts with very widely different results on the same specimen).

neo*Tenulin and Derivatives.*—Tenulin (250 mg.) in distilled water (25 ml.) and saturated aqueous sodium hydrogen carbonate solution (2 ml.) was heated on the steam-bath for 2½ hr. (prior investigation had shown that this was the optimum time). Extraction with chloroform afforded *deacetylneotenulin*, m. p. (from chloroform–benzene–light petroleum) 239—242°, $[\alpha]_D$ −27° (*c* 1·04), $\lambda_{max.}$ 240 mμ (ε 16,000) (Found : C, 67·85; H, 7·55. $C_{15}H_{20}O_4$ requires C, 68·15; H, 7·65%). Acetylation with pyridine–acetic anhydride overnight at room temperature afforded neo*tenulin*, m. p. (from aqueous methanol) 193—193·5°, $[\alpha]_D$ −23° (*c* 0·93), $\lambda_{max.}$ 239 mμ (ε 15,000) (Found : C, 66·2; H, 7·45. $C_{17}H_{22}O_5$ requires C, 66·65; H, 7·25%). Chromatography of the combined mother-liquors from the preparation of deacetyl*neo*tenulin over neutral deactivated alumina (2 g.) gave, on elution with benzene, deacetyl*iso*tenulin, m. p. 251—253°, $[\alpha]_D$ −20° (*c* 1·09), $\lambda_{max.}$ 225 mμ (ε 8500), identical (mixed m. p. and the same physical properties) with a specimen prepared (Clark, *loc. cit.*) from *iso*tenulin by acid hydrolysis.

Deacetyl*neo*tenulin (96 mg.) in chloroform (25 ml.) was ozonised at 0° for 4 hr. (disappearance of ultraviolet absorption maximum). Water (25 ml.) was added and the mixture distilled. Neutralisation (aqueous sodium hydroxide) of the distillate, removal of the chloroform, and treatment with *p*-bromophenacyl bromide in the usual way gave after chromatography *p*-bromophenacyl acetate (27 mg.), identified by m. p., mixed m. p., and analysis (Found : C, 46·9; H, 3·6. Calc. for $C_{10}H_9O_3Br$: C, 46·7; H, 3·5%).

Deacetyl*neo*tenulin (220 mg.) was treated with chromic acid in " AnalaR " acetic acid (20 ml.; 0·25N) at room temperature. After 1 hr. the uptake of chromic acid corresponded to 0·9 atom of " oxygen." Isolation of the product in the usual way gave *deacetyldehydroneotenulin*, m. p. (from benzene–light petroleum) 178—182° (somewhat variable), $[\alpha]_D$ −164° (*c* 1·30), −164° (*c* 1·28), $\lambda_{max.}$ 245 mμ (ε 12,000), ε 6000 at 229 and 257 mμ (Found : C, 68·8; H, 7·35. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%). Cholest-4-ene-3 : 6-dione has $\lambda_{max.}$ 254 mμ (ε 10,000), ε 5000 at 226 and 270 mμ : the latter compound had a much wider band, apart from a maximum at longer wavelength, as shown by the band width at half the maximum intensity.

The diketone (5 mg.) was dissolved in acetic acid (0·5 ml.), zinc (200 mg.) added, and the

mixture heated on the steam-bath, with occasional stirring, for 1 hr. At the end of this time the spectrum of the isolated material was essentially unchanged.

Deacetyldehydroisotenulin.—Deacetyl*iso*tenulin (see above) (109 mg.) was treated with chromic acid in " AnalaR " acetic acid (11 ml.; 0·13N) at room temperature for 90 min. Crystallisation of the product from benzene–light petroleum gave *deacetyldehydroisotenulin*, plates, m. p. 223—224°, $[\alpha]_D$ −209° (*c* 0·90), $\lambda_{max.}$ 228 mμ (ε 8000) (Found : C, 68·45; H, 7·2. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%).

Deacetyldihydroisotenulin.—This compound was best prepared as follows (cf. Clark, *loc. cit.*). Dihydro*iso*tenulin (see above) (480 mg.) was refluxed with water (80 ml.) and saturated aqueous sodium hydrogen carbonate (20 ml.) for 2 hr. On cooling, deacetyldihydro*iso*tenulin (280 mg.) crystallised, m. p. 202—203°, $[\alpha]_D$ +151° (*c* 0·80). The 2 : 4-*dinitrophenylhydrazone*, prepared in the usual way and chromatographed over kieselguhr–bentonite (Elvidge and Whalley, *Chem. and Ind.*, 1955, 589), had m. p. (from methanol) 276—277° (Found : C, 56·9; H, 5·9; N, 12·0. $C_{21}H_{26}O_7N_4$ requires C, 56·5; H, 5·85; N, 12·55%). The *oxime*, prepared with pyridine–hydroxylamine hydrochloride overnight at room temperature, had m. p. (from methanol) 246—248° (Found : N, 5·65. $C_{15}H_{23}O_4N$ requires N, 5·0%).

Dehydrogenations.—(*a*) *iso*Tenulin (1·5 g.) in ethanol (10 ml.) was treated with potassium borohydride (1·0 g.) in water (2 ml.) for 1 hr. The total product was dehydrogenated in 100-mg. portions by 10% palladised charcoal (100 mg.) under nitrogen at 320° for 15 min. The combined dehydrogenated product was filtered in light petroleum (b. p. 60—80°) solution through neutral deactivated alumina (3 g.) and the azulene fraction was extracted with 90% phosphoric acid. Recovery from phosphoric acid into light petroleum solution by addition of water gave (by the absorption spectrum) about 3 mg. of azulene. The theoretical amount of 1 : 3 : 5-trinitrobenzene was added and the adduct, crystallised from light petroleum (b. p. 60—80°) and then from methanol, was identified as the chamazulene derivative by crystal form, m. p., mixed m. p., and ultraviolet and visible absorption spectra (identical at all wavelengths) (for spectra of azulenes see Takeda, Kubota, and Nagata, *Pharm. Bull.*, 1953, **1**, 241).

(*b*) *iso*Tenulin (1·7 g.) was converted into dihydro*iso*tenulin (see above), and the total product reduced with lithium aluminium hydride (900 mg.) in dry ether (200 ml.) under reflux for 2 hr. Decomposition of the excess of lithium aluminium hydride with ethyl acetate and dilute aqueous hydrochloric acid, followed by extraction with chloroform (5 × 10 ml.) and ether (5 × 10 ml.), gave a semicrystalline product (1·3 g.). This was dehydrogenated in 200-mg. portions by 10% palladised charcoal (200 mg.) under nitrogen at 320° for 15 min. The dehydrogenated product was worked up as above to give approx. 1·5 mg. of azulene. The derived 1 : 3 : 5-trinitrobenzene adduct had m. p. 155—157°. It was largely depressed (25°) with the S-guaiazulene adduct (m. p. 150—152°), but did not depress the m. p. of linderazulene 1 : 3 : 5-trinitrobenzene adduct (m. p. 153—157°).

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28. *Chemistry of Nitrosyl Complexes. Part II.* Exchange of* ^{36}Cl *between Nitrosyl Chloride and Some Insoluble Metal Chlorides.*

By J. Lewis and D. B. Sowerby.

The exchange of radioactive chlorine (^{36}Cl) between zinc, mercury, and cadmium chlorides on the one hand, and liquid nitrosyl chloride on the other, has been studied. Rapid exchange occurs between the absorbed nitrosyl chloride and the metal chloride, followed by a slow heterogeneous exchange with the excess of solvent. The results are considered to favour the formation of unstable nitrosonium salts of the metal chlorides. The path for the heterogeneous exchange is the decomposition of the nitrosonium salt, and in agreement with this no exchange was found when a stable nitrosonium salt, nitrosonium chlorostannate, or chlorides that do not form complexes with nitrosyl chloride, *e.g.*, sodium or potassium chloride, were studied. Silver chloride does not form a complex with the nitrosyl chloride, no exchange being observed in the dark, but a slow heterogeneous exchange occurs in the light.

Nitrosyl chloride forms the following addition compounds with metals of the last two sub-groups of the transition metals: $CuCl,NOCl$; $ZnCl_2,NOCl$; $AuCl_3,NOCl$; $HgCl_2,NOCl$. Cadmium and silver chlorides have not been reported to form compounds, and the nature of the bonding of the nitrosyl chloride in the copper, zinc, and mercury chloride complexes is not known. Asmussen [1] and previous workers consider that the zinc and mercury compounds are best represented as loose addition complexes, as the nitrosyl chloride may be removed completely by gentle heat or by applying a vacuum. Addison and Lewis [2] have suggested that they may be nitrosonium chloro-complexes involving a polymeric complex ion. In order to obtain information on the bonding in these complexes, and to determine if compound formation occurs with silver and cadmium chlorides, we have investigated the exchange of radioactive chlorine (^{36}Cl) between nitrosyl chloride and the metal chlorides. The easy removal of nitrosyl chloride from these complexes affords a ready method for the study of the equivalence of the chlorine atoms in the compounds.

Experimental

Preparation of Compounds containing ^{36}Cl.—Nitrosyl chloride (15 ml.), prepared as described in Part I,* was condensed directly on to approx. 0·2 g. of active tetramethylammonium chloride. Exchange was complete within the time of separation at $-5°$ and the active nitrosyl chloride was distilled off.

Zinc chloride. Active nitrosyl chloride was condensed on to a block of zinc, suspended on a glass hook. The temperature was allowed to rise slowly from $-40°$ to room temperature. The zinc block was removed and the yellow complex formed, $ZnCl_2,NOCl$, was heated on an oil-bath at 120° for 30 min., giving a white powder (Found: Zn, as quinaldinate, 47·9; Cl, 51·9. Calc. for $ZnCl_2$: Zn, 48·0; Cl, 52·0%).

Cadmium chloride. Cadmium carbonate (approx. 8 g.) was added to 10 ml. of 11N-hydrochloric acid containing 0·1 ml. of $H^{36}Cl$ till a neutral solution was obtained. The solution was evaporated on a water-bath, and on cooling crystals of $CdCl_2,H_2O$ separated, and were then [3] heated in a stream of nitrogen at 120—140° for 3 hr. (Found: Cl, 38·8. Calc. for $CdCl_2$: 38·7%).

Mercuric chloride. Excess of active nitrosyl chloride was condensed on to 0·5 g. of mercury at $-40°$, and the temperature allowed to rise slowly. The compound was treated with another portion of active nitrosyl chloride to ensure that there was no unchanged mercury present. The yellow $HgCl_2,NOCl$ formed was heated on a water-bath for 30 min. to give mercuric chloride (Found: Cl, 26·10. Calc. for $HgCl_2$: Cl, 26·15%).

Silver chloride. Hydrochloric acid (10 ml., containing $H^{36}Cl$) was treated with excess of

* Part I, *J.*, 1955, 56.

[1] Asmussen, *Z. anorg. Chem.*, 1939, **243**, 127.
[2] Addison and Lewis, *J.*, 1951, 2843.
[3] Cf. Lister and Sutton, *Trans. Faraday Soc.*, 1941, **37**, 406.

silver nitrate solution, and the precipitated silver chloride was centrifuged, washed with water, alcohol, and ether, and dried at 120° in a vacuum.

Sodium chloride and potassium chloride. Hydrochloric acid (2 ml., containing $H^{36}Cl$) was neutralised with 2·98N-sodium hydroxide and gently evaporated to dryness; the active sodium chloride was dried in a vacuum (P_2O_5) for 6 hr. at 120°. Active potassium chloride was similarly prepared.

Nitrosonium chlorostannate. Excess of active nitrosyl chloride was condensed on to redistilled stannic chloride (1·5 ml.) at −30°. The temperature was allowed to rise slowly to −5°. If any stannic chloride remained unchanged the product fumed in the air; further treatment with active nitrosyl chloride gave a yellow product, not fuming in the air [Found : Cl, 54·2. Calc. for $(NO)_2SnCl_6$: Cl, 54·3].

In the preparation of zinc chloride, mercuric chloride, and nitrosonium hexachlorostannate, moisture was rigidly excluded. The preparations were carried out in B14 flasks fitted with guard tubes of phosphoric oxide. All the preparations were subsequently handled in a Towers Manipulator Box.

Exchange Runs.—Exchange runs were carried out essentially as described in Part I. A known weight of the metal chloride was added through a side-arm to liquid nitrosyl chloride, which was fractionally distilled into the exchange vessel to a calibrated mark. The liquid was stirred by manual magnetic stirring to ensure complete mixing. Known fractions of nitrosyl chloride were distilled from the exchange vessel after various time intervals. It was important in all experiments to use finely divided solids, as incomplete reaction was observed with coarsely powdered samples.

The activity of the samples was determined by precipitating the chloride as silver chloride and matting this to infinite thickness on G.E.C. 1·5-cm. planchets. Allowance was made for the background count.

The initial activity of the metal chloride was found by hydrolysing the compound in dilute aqueous sodium hydroxide and precipitation of the chloride as silver chloride; the final activity was obtained from the metal chloride remaining in the exchange vessel after all excess of nitrosyl chloride had been removed.

In the heterogeneous studies, it was found more accurate to use active metal chloride, and determine the rate of attainment of activity of the nitrosyl chloride. Use of active nitrosyl chloride and determination of the rate of fall in activity usually involved small changes, as a large excess of nitrosyl chloride was employed in the experiments.

Results and Discussion

All the metal chlorides except auric chloride are insoluble in liquid nitrosyl chloride. Therefore the exchange reactions with nitrosyl chloride may be considered in two parts : (*a*) the exchange of the combined nitrosyl chloride with the metal chloride, (*b*) the heterogeneous exchange of the chloride, or addition complex if formed, with the liquid nitrosyl chloride. Exchange of the chloride in the copper complex was not carried out, as the compound decomposed very rapidly to a mixture of cuprous and cupric chloride, even in the absence of light.

Table 1 contains typical values for the exchange of nitrosyl chloride with the metal

Table 1. *Exchange of nitrosyl chloride with zinc, mercury, cadmium, and silver chlorides.* (Temp. −15°).

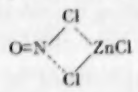
Metal chloride	Expt. no.	Required for 1 : 1 compound (counts/min.)	Found (counts/min.)	Time of contact (min.)
$ZnCl_2$	(i)	570	565	263
	(ii)	821	808	44
	(iii)	240	234 *	5
	(iv)	570	541	5 (in dark)
$HgCl_2$	(i)	399	320	30
	(ii)	524	500 *	5
	(iii)	634	616	5 (in dark)
$CdCl_2$	(i)	186	259	5
	(ii)	309	340	5 (in dark)
AgCl	(i)	270	400	90 (in dark)

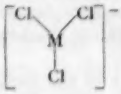
* Using active NOCl and inactive complex.

chlorides. The change in activity of chloride in zinc and mercury chlorides agrees with the formation of a 1 : 1 complex, in which the chlorine rapidly exchanges with the combined nitrosyl chloride. After allowance has been made for the heterogeneous exchange, by determining the activity of the supernatant nitrosyl chloride, values of the exchange showed that no higher complex than a 1 : 1 complex is formed during 6 hr.

The experiments with zinc and mercuric chloride in the dark showed that the exchange was not photochemical. Experiments were carried out using both active metal chloride and active nitrosyl chloride. The change in activity corresponded to partial compound formation in the case of cadmium chloride, but no compound formation with silver chloride for reactions carried out in the dark. If a 1 : 1 complex is assumed with cadmium chloride and nitrosyl chloride, a 60% conversion into the complex occurs; this incomplete formation may be associated with the protective nature of the film formed when metallic cadmium react with nitrosyl chloride. Zinc and mercury react rapidly to form the metal chloride–nitrosyl chloride complex, but the reaction with cadmium is very quickly inhibited by the formation of a protective film of chloride over the metal surface. We were not able to isolate any compound with cadmium chloride, for the nitrosyl chloride is completely removed from the product on standing at room temperature.

The rapid exchange indicates that the nitrosyl chloride is combined with the metal chloride and does not correspond to a physical absorption of the gas into chloride lattice. The complex may be formulated as (I) or (II). Structure (I) would give a fall of 25% in

(I) 

[NO⁺] 

(II)

the activity of the metal chloride, and to account for the observed fall of *ca.* 33% would require the breaking and formation of a number of zinc–chlorine bonds. The complex involves the bonding of two chlorine atoms to a nitrogen atom which, as discussed in Part I, is considered unlikely. The change in activity is readily explained by structure (II), in which a nitrosonium compound is formed. The complexes would then correspond to nitrosyl chloride complexes of many other metal chlorides, which have been established as nitrosonium chloro-complexes.[4]

The ions $(ZnCl_3)^-$, $(CdCl_3)^-$, and $(HgCl_3)^-$ have been established in melts of alkali-metal chlorides with the corresponding metal chloride.[5] The stability of the compounds is found to depend upon the radius of the alkali-metal ion. No complexes are formed with lithium chloride, but sodium chloride gives a compound with an inconguent melting point, and potassium, rubidium, and ammonium chlorides give compounds with a congruent melting point. The radius[6] of the nitrosonium ion is 1·40 Å, compared[7] with potassium 1·33 Å and rubidium 1·48 Å; hence, from these considerations compound formation to give the $(MCl_3)^-$ ion is possible.

The ion $(MCl_3)^-$ is polymeric in structure, with each metal atom surrounded by six chloride ions, *i.e.*, a distorted perovskite structure.[8] The $(MCl_3)^-$ ion which occurs in aqueous solution is presumably tetrahedral in structure, the fourth position being occupied by a water molecule, as these complexes are usually monohydrated. In agreement with this polymeric structure of the $(MCl_3)^-$ ion is the insolubility of the complexes in liquid nitrosyl chloride. This formulation of the complex is also related to the behaviour of zinc and mercury chloride in other chloro-solvent systems. With strong chloro-donor compounds insoluble complexes are formed; *e.g.*, with phosphorus pentachloride. Groeneveld[9] has isolated 1 : 1 complexes which have been shown to be salts, $(PCl_4)^+(MCl_3)^-$.

Heterogeneous Exchange.—In addition to the exchange of the combined nitrosyl chloride

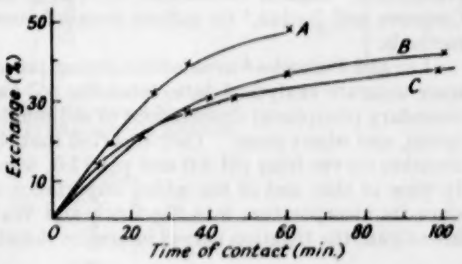
[4] Addison and Lewis, *Quart. Rev.*, 1955, **9**, 115.
[5] Belyaev and Mironov, *Zhur. obschei Khim.*, 1952, **22**, 1734; Bloom and Heymann, *Proc. Roy. Soc.*, 1947, *A*, **188**, 392.
[6] Ketelaar and Palmer, *J. Amer. Chem. Soc.*, 1937, **59**, 2629.
[7] Wells, "Structural Inorganic Chemistry," Oxford, 2nd edn., 1950, p. 70.
[8] *Idem, op. cit.*, p. 290.
[9] Groeneveld, *Rec. Trav. chim.*, 1952, **71**, 152.

with the metal chloride, a slow heterogeneous exchange occurs between the solvent and the complex. Values for this exchange are shown in the figure. The percentage exchange for the cadmium complex was calculated on the assumption of 100% compound formation, so the actual values are in excess of those shown. The rates of the reactions were found to depend on the degree of division of the solids, and were not photochemical. A possible path for the exchange is the formation of the addition complex with exchange of the chlorine atoms, as discussed above, followed by dissociation of the complex and slow transference of the activity to the solution.* When chlorides which did not form complexes with nitrosyl chloride, or which formed very stable nitrosonium chloro-complexes, were studied, no exchange was observed with liquid nitrosyl chloride. Table 2 gives the values

TABLE 2. *Exchange of nitrosyl chloride with metal chlorides.*

Compound	Temp.	Time of contact (min.)	Activity of NOCl for 100% exchange (counts/min.)	Activity of NOCl (counts/min.)
NaCl	−10°	240	210	3
	−10	310	342	0
KCl	−20	360	197	2
$[NO]_2^+[SnCl_6]^=$	−20	90	410	3
	−15	303	205	0

of the exchange for sodium and potassium chloride and for nitrosonium chlorostannate, which is the most stable nitrosyl chloride addition compound known [10] and has been shown by Klinkenberg [11] to be a true salt. Thus the dissociation to nitrosyl chloride,



Heterogeneous exchange between solvent and complex.

A, $CdCl_2$,NOCl.
B, $HgCl_2$,NOCl.
C, $ZnCl_2$,NOCl.

responsible for the exchange with the zinc, cadmium, and mercury chlorides, will not occur. In the case of hydrogen chloride and stannic chloride, however, rapid exchange of chloride has been observed for solid, liquid, and gaseous stannic chloride with gaseous hydrogen chloride; [12] the complex, $SnCl_4$,2HCl, is very unstable and readily dissociates and forms an obvious path for the exchange.

Silver chloride was found to exchange with liquid nitrosyl chloride in the presence of light, but no exchange was observed in the dark (see Table 1). The photochemical decomposition of silver chloride and nitrosyl chloride is the probable path of the exchange reaction.

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THE UNIVERSITY, SHEFFIELD, 10. [*Received, July 4th, 1955.*]

* These differences in the rate of reaction of heterogeneous systems may be accounted for alternatively by changes in the nature and area of the surfaces of the solids.

[10] Whynes, Thesis, London, 1948.
[11] Klinkenberg, *Rec. Trav. chim.*, 1937, **56**, 749.
[12] Howald and Willard, *J. Amer. Chem. Soc.*, 1955, **77**, 2046.

29. *Deoxypentose Nucleic Acids. Part VII.* A Re-examination of the Titration Curves of Sodium Deoxyribonucleate.*

By D. O. Jordan, A. R. Mathieson, and Sheila Matty.

The anomalous electrometric titration of sodium deoxyribonucleate has been re-examined and the pG' values of the titrating groups have been calculated for the forward as well as the backward titration. An explanation for the change in the pG' values from forward to backward titration is given on the basis of the hydrogen-bond hypothesis. The difference between the backward titration curves from pH 2 and pH 12 is confirmed.

The application of electrometric titration to the study of nucleic acids has yielded significant results. Gulland, Jordan, and Taylor [1] found that the forward titration curves of sodium deoxyribonucleate of calf thymus from the neutral region to pH 2·0 and pH 12·0 differed from the curve obtained on backward titration from these extremes of pH. They suggested that this "hysteresis" effect might be due to the existence of hydrogen bonding between different titrating groups, which would influence the forward titration curves. This bonding is an integral feature of the structure recently put forward for nucleic acid by Crick and Watson.[2] The backward titration curves were interpreted by Gulland *et al.* as indicating one equivalent each of the amino-dissociations of guanine, adenine, and cytosine, and 0·25 equivalent of secondary phosphoryl dissociations for every 4 atoms of phosphorus. Similar conclusions have been reached by Signer and Schwander,[3] and by Cosgrove and Jordan,[4] for sodium deoxyribonucleate from other sources isolated by other methods.

Lee and Peacocke [5] avoided the drying procedure used by Gulland *et al.* and, employing more accurate analytical data, listed the pG' values of the guanine, adenine, cytosine, and secondary phosphoryl dissociations of sodium deoxyribonucleate from calf thymus, herring sperm, and wheat germ. They reported that there was a difference between the backward titration curves from pH 2·0 and pH 12·0, which Gulland *et al.* had found to be identical. In view of this, and of the added importance acquired by the hydrogen-bond hypothesis since its incorporation into the Crick and Watson structure, it was thought desirable to investigate the titration curves in greater detail, particularly the forward curve.

Results.—Fig. 1 shows a typical titration curve for sodium deoxyribonucleate. Fig. 2 shows in greater detail a number of forward titration curves in the acid region at different concentrations of sodium deoxyribonucleate.

Analysis of the titration curves in the acid region. It is possible [6] to represent the titration curve of a polybasic acid by a series of titration constants, G_1'. To achieve reasonably precise pG' values it is necessary to know accurately the analytical proportions of the different titrated groups. Such analytical data have only recently become available, through the chromatographic studies of Markham and Smith,[7] Wyatt,[8] and Chargaff, Zamenhof, and Green,[9] who conclude that the composition of deoxyribonucleic acid does not vary in different tissues of the same species. We have employed Wyatt's analytical figures for calf-thymus nucleic acid, 1·13 moles of adenine, 0·86 of guanine, 0·85 of cytosine, and 1·11 of thymine per 4 g.-atoms of phosphorus.

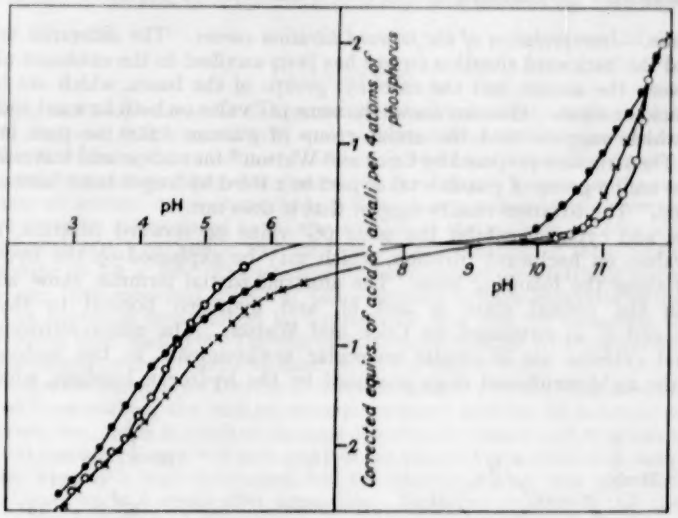
The detailed shape of the forward titration curves shown in Fig. 2 indicates that the pG'

* Part VI, *J.*, 1949, 1413.

[1] Gulland, Jordan and Taylor, *J.*, 1947, 1131.
[2] Crick and Watson, *Proc. Roy. Soc.*, 1954, *A*, **223**, 80.
[3] Signer and Schwander, *Helv. Chim. Acta*, 1949, **32**, 853.
[4] Cosgrove and Jordan, *J.*, 1949, 1413.
[5] Lee and Peacocke, *J.*, 1951, 2361.
[6] Simms, *J. Amer. Chem. Soc.*, 1926, **48**, 1239; Cohn and Edsall, "Proteins, Amino Acids, and Peptides," Reinhold Publ. Corp., New York, 1943, p. 451.
[7] Markham and Smith, *Biochem. J.*, 1949, **45**, 294.
[8] Wyatt, *ibid.*, 1951, **48**, 584.
[9] Chargaff, Zamenhof, and Green, *Nature*, 1950 **165**, 756.

values of the bases titrating in the acid region are markedly different from those calculated from the backward curves. In particular, an inflection is present in the forward curves near pH 4, which suggests that the pG' values of guanine and adenine are appreciably further apart than

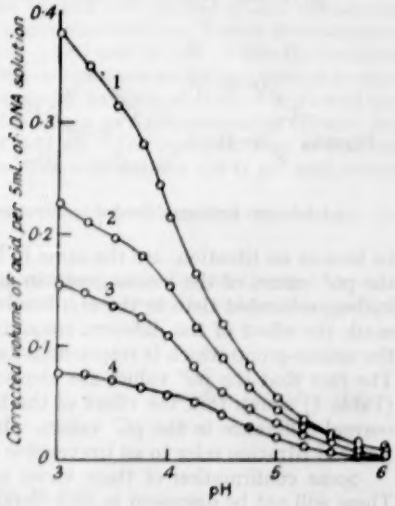
FIG. 1. *Titration of sodium deoxyribonucleate.*



○ *Titration from* pH 7·00 (*forward titration*).
× *Titration from* pH 2·50 (*backward titration*).
● *Titration from* pH 12·00 (*backward titration*).

FIG. 2. *Forward titration in the acid region at different nucleate concentrations* (C).

1, C = 18·75;
2, C = 11·25;
3, C = 7·50;
4, C = 3·75 (C *in* 10^{-4} *equiv. of* 4P *atoms per l.*).



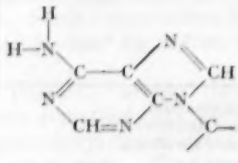
those calculated from the backward curves. This inflection occurs at higher pH values at lower concentrations of sodium deoxyribonucleate, which is to be expected from the effect of concentration on the pG' values reported in Part VIII (following paper). The initial steepness of the forward titration curves suggests that the pG' values of adenine and cytosine are much closer together than those calculated from the backward curves, which is fully supported by the

pG' values of the bases calculated from the forward titration curves, shown in the Table together with the corresponding pG' values calculated from the backward titration curves.

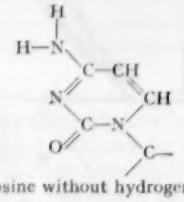
	Guanine	Adenine	Cytosine
pG': forward titration	2·50	4·40	4·40
„ backward „	2·40	3·65	4·85

Discussion.—Interpretation of the forward titration curves. The difference between the forward and the backward titration curves has been ascribed to the existence of hydrogen bonds between the amino- and the carbonyl groups of the bases, which are irreversibly broken by acid or alkali. Guanine shows the same pG' value on both forward and backward titration, which suggests that the amino-group of guanine takes no part in hydrogen bonding. The structure proposed by Crick and Watson [2] for nucleic acid leaves it uncertain whether the amino-group of guanine takes part in a third hydrogen bond between guanine and cytosine. The titration results suggest that it does not.

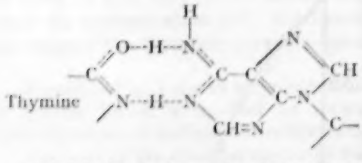
Adenine and cytosine exhibit the same pG' value on forward titration, but widely different values on backward titration, which may be explained on the hydrogen-bond hypothesis along the following lines. The annexed partial formulæ show adenine and cytosine in the normal state (*a* and *b*), and hydrogen bonded to thymine and guanine (*c* and *d*) as envisaged by Crick and Watson. The amino-nitrogen atoms of adenine and cytosine are in similar molecular environments in the hydrogen-bonded forms, as the eight-membered rings produced by the hydrogen bonding, which have to



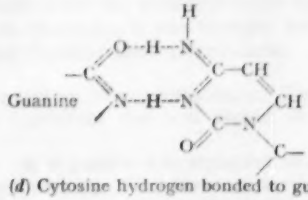
(*a*) Adenine without hydrogen bonds.



(*b*) Cytosine without hydrogen bonds.



(*c*) Adenine hydrogen bonded to thymine.



(*d*) Cytosine hydrogen bonded to guanine

be broken on titration, are the same in both cases. It is therefore to be expected that the pG' values of the amino-group in adenine and cytosine will be closer together in the hydrogen-bonded than in the non-bonded forms, since the hydrogen bonding will tend to mask the effect of the different resonating ring systems on the dissociation properties of the amino-group which is responsible for the different pG' values of adenine and cytosine. The fact that the pG' values are identical as calculated from the forward titration curve (Table 1) shows that the effect of the hydrogen-bonded rings is to mask completely this normal difference in the pG' values. It should be pointed out that these pG' values on forward titration refer to an irreversible change in the system.

Some confirmation of these views is to be obtained from the alkali-titration curves. These will not be discussed in such detail since they cannot be interpreted with confidence owing to the difficulty of making accurate calculations of the water correction at the highest pH. Nevertheless it is clear that the pG' values of the dissociating groups are much closer together on forward than on backward titration, and it is possible in consequence that this may be interpreted similarly.

The backward titration curves from pH 2 *and* pH 12. Fig. 1 shows that the backward

titration curves obtained by titration from pH 2 with alkali and from pH 12 with acid are not coincident, in agreement with Lee and Peacocke's results.[5] No satisfactory explanation of this effect has yet been found, but it is hoped that studies of the thermal and alkaline degradation of sodium deoxyribonucleate, and of the influence of pH on the streaming birefringence and electrophoretic mobility, now proceeding, may be of assistance in this.

Experimental

Preparation and Properties of the Sodium Deoxyribonucleate.—The samples of sodium deoxyribonucleate employed [G1(i) and G1(ii)] were extracted from calf-thymus tissue by the late R. H. Garner, B.Sc., using the procedure of Gulland, Jordan, and Threlfall.[10] A single specimen of nucleoprotein was obtained from the glands, and divided into 2 parts for the preparation of the 2 samples of sodium deoxyribonucleate. G1(ii) has a sedimentation constant (S^0_{20}) in 0·2M-sodium chloride, extrapolated to infinite dilution of the nucleate, of $15{\cdot}4 \times 10^{-13}$, and a diffusion constant (D^0_{20}) of $1{\cdot}06 \times 10^{-6}$ cm.^{2} sec.$^{-1}$. Combination of these results gives [11] a molecular weight of $7{\cdot}9 \times 10^6$. The rotary diffusion constant, and intrinsic viscosity at zero shear have also been measured for G1(i) and combined to give estimates of its molecular weight.[12] The fractional precipitation by hydrochloric acid and the streaming birefringence of G1(i) have also been studied.[13] The two samples gave identical titration curves within the limits of experimental error. They contained N, 15·7%, and P, 8·8%.

Preparation of the Solutions for Titration.—Stock solution (0·3%) of sodium deoxyribonucleate was prepared by dissolving the undried material, without stirring, in water of conductivity approx. 10^{-6} mho/ml., made in a still of the type described by Stuart and Wormwell,[14] and was kept at 0°. It has been shown [11,15] that many of the physical properties of sodium deoxyribonucleate alter when it is kept in solution, but the titration curves were reproducible within experimental error up to 6 weeks after dissolution. Measured portions of this stock solution were taken and made up to 5 ml. for titration.

Titration Procedure.—The cell consisted of a hydrogen and a standard silver–silver chloride electrode, the two compartments being connected with a saturated potassium chloride–agar salt bridge. The solutions were kept sufficiently stirred by the hydrogen bubbling over the electrode. Two platinum electrodes were kept in the solution and checked against one another from time to time during the titration. The E.M.F.'s were measured on a Tinsley potentiometer, and readings were estimated to be accurate to at least ±0·01 unit of pH. 0·05N-Hydrochloric acid and -sodium hydroxide were used except when the volume to be added was such as to make the volume change too great to be corrected accurately by Taylor's method; [16] 0·5N-acid and -alkali were then used. The acid and alkali were added from an Agla micrometer syringe, and E.M.F. readings were taken after each addition of 0·01 ml. The reproducibility of titration curves obtained on solutions prepared from the same stock solution was ±0·01 pH unit, except in the neutral region.

The concentration of nucleate in the stock solution was determined by analysis for phosphorus.[17]

With respect to this and the following paper we thank the British Empire Cancer Campaign (Nottinghamshire Branch) for financial help with the cost of this research, and for the award of a bursary (to S. M.).

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[*Received, July 15th*, 1955.]

[10] Gulland, Jordan, and Threlfall, *J.*, 1947, 1129.
[11] Howard, Thesis, Nottingham, 1953.
[12] Mathieson and Porter, *Biochim. Biophys. Acta*, 1954, **14**, 288.
[13] *Idem*, *Nature*, 1954, **173**, 1190.
[14] Stuart and Wormwell, *J.*, 1930, 85.
[15] Sadron, *Progr. Biophysics Biophys. Chem.*, 1953, **3**, 237;
[16] Jordan and Taylor, *J.*, 1946, 994.
[17] Jones, Lee, and Peacocke, *J.*, 1951, 623.

30. *Deoxypentose Nucleic Acids. Part VIII.* The Influence of Concentration and Ionic Strength on the Electrometric Titration of Sodium Deoxyribonucleate.*

By D. O. Jordan, A. R. Mathieson, and Sheila Matty.

The titration curves of sodium deoxyribonucleate have been determined at different concentrations and in solutions of different ionic strengths, and a titration curve extrapolated to zero concentration and ionic strength has been obtained. These curves have been analysed and the influence of the concentration and ionic strength on the dissociation constants of the titrating groups determined. From the curve at zero concentration and ionic strength the thermodynamic dissociation constants of the titrating groups have been calculated. The electric charge carried by the nucleate ion has been calculated for solutions of different pH, concentration, and ionic strength. The influence of concentration and ionic strength on the difference between the forward and the backward titration curves has been examined.

Recent theoretical and experimental work on polyelectrolytes has shown that the apparent titration constant (pG') of a dissociating group in the polymer is strongly dependent on the concentration of the polymer and the ionic strength of the solution.[1] The results of an investigation of the effect of varying the concentration and the ionic strength of the solution on the electrometric titration of sodium deoxyribonucleate of calf thymus are reported here. In addition to the thermodynamic dissociation constants (pK_0) of the dissociating groups, it was hoped to obtain an estimate of the charge carried by the nucleate ion which could be compared with similar calculations from electrophoretic results to be reported later. A comparison of the effects of concentration and of ionic strength on the titration curves might also indicate the form of the relation between the concentration of a polyion and the ionic strength of a simple electrolyte. Also, it was hoped to obtain further information on the hydrogen bonding and intermolecular interactions in sodium deoxyribonucleate from the effect of ionic strength and concentration on the difference between the forward titration curves from the neutral region and the backward titration curves from the extremes of pH. The sample of nucleate employed [G1(ii)] has been described in Part VII (preceding paper).

Results

Effect of Ionic Strength on the Titration Curves.—Lithium chloride was used for variation of the ionic strength of the nucleate solutions because its high solubility made it possible to raise the ionic strength (I) of the solutions without greatly altering their volumes. A series of solutions of sodium deoxyribonucleate of the same concentration (0·00142 equiv. of P per l.) were brought to pH 12·00 by the addition of 0·5N-sodium hydroxide, and then different amounts of 0·5N-hydrochloric acid were added to give the solutions different pH values in the range pH 3—12. These solutions were then titrated with 12·228M-lithium chloride; the results, plotted as pH versus $\sqrt{I}$, are shown in Fig. 1. Titration curves at constant ionic strength may be obtained from these curves, which describe the effect of ionic strength on the backward titration curve of sodium deoxyribonucleate. A few similar results on the forward titration curve are shown in Fig. 2. For these experiments the initial addition of sodium hydroxide to bring the solutions to pH 12 was omitted. No evidence was obtained that lithium chloride influences the hydrogen bonds. By titration with lithium chloride rather than with acid or alkali, titration curves at constant ionic strength were obtained by rapid continuous titration, instead of having to make up the solution separately for each point on the titration curve. Also, it disposed of difficulties associated with the precipitation of the nucleate in salt solution on the addition of acid.

* Part VII, preceding paper.

[1] Katchalsky *et al.*, *J. Polymer Sci.*, 1947, **2**, 432; 1950, **5**, 283; 1954, **12**, 159; Arnold and Overbeek *Rec. Trav. chim.*, 1950, **69**, 192.

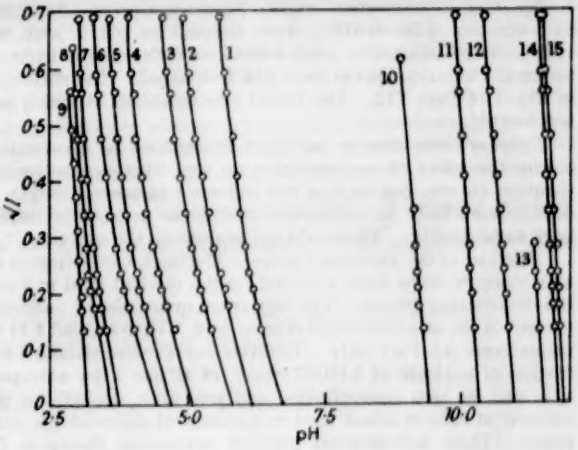
FIG. 1. *Effect of ionic strength on the* pH *of nucleate solutions on backward titration.*

Normality of HCl *present*:

1, 0;
2, 0·00025;
3, 0·0005;
4, 0·001;
5, 0·0015;
6, 0·002;
7, 0·0025;
8, 0·003;
9, 0·004.

Normality of NaOH *present*:

1, 0;
10, 0·00075;
11, 0·002;
12, 0·004;
13, 0·005;
14, 0·0095;
15, 0·0125.



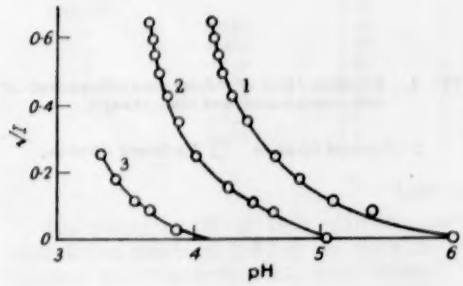


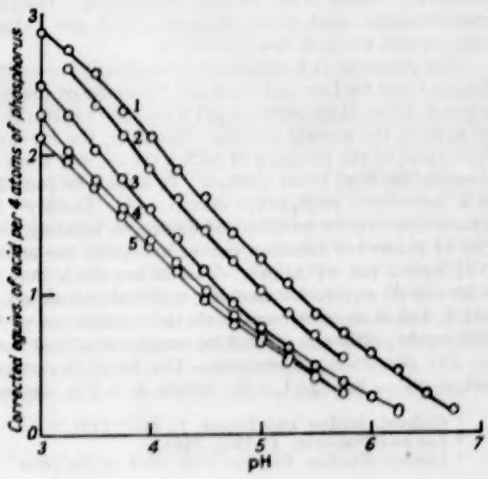
FIG. 2. *Effect of ionic strength on the* pH *on forward titration on the acid side.*

Normality of HCl *present*:

1, 0;
2, 0·0005;
3, 0·002.

FIG. 3. *Backward titration curves in the acid region at different nucleate concentrations* (*C*).

1, $C = 1{\cdot}13$;
2, $C = 1{\cdot}88$;
3, $C = 2{\cdot}81$;
4, $C = 3{\cdot}75$;
5, $C = 11{\cdot}25$ (*C* in 10^{-4} equiv. of 4P atoms per l.).



Effect of Concentration on the Titration Curves.—Sodium deoxyribonucleate solutions of concentration 0·26—0·016% were titrated to pH 2 with 0·05N- or 0·5N-hydrochloric acid, and back to neutrality with 0·05N- or 0·5N-sodium hydroxide, Fig. 3 shows some of the backward titration curves from pH 2 obtained. The corresponding forward curves are shown in Fig. 1 of Part VII. The lowest concentration at which accurate results could be obtained was 0·016%.

Effect of Concentration and Ionic Strength on the Hysteresis.—The same curves were used to obtain the effect of concentration on the difference between the forward and the backward titration curves, but to find the influence of ionic strength on this hysteresis effect, sodium deoxyribonucleate in concentrated aqueous potassium chloride was titrated to pH 12 and back to neutrality. This could not be done on the acid side.

Analysis of the Titration Curves.—The backward titration curves at different ionic strengths and concentrations were analysed by the method used in Part VII to obtain the pG' values of the dissociating groups. The analytical quantities of guanine, adenine, cytosine, and thymine present in the nucleate were taken as 0·86, 1·13, 0·85, and 1·11 mole per 4 g.-atoms of phosphorus, respectively (cf. Part VII). Titration curves were obtained for zero ionic strength at a concentration of nucleate of 0·00142 equiv. of 4P per l. by extrapolation of the plots of pH against $\sqrt{I}$, and for zero concentration and zero ionic strength by plotting concentration against the amount of acid or alkali used in titration at different pH values and taking the slopes at the origin. These extrapolated titration curves are shown in Fig. 4. They were also analysed

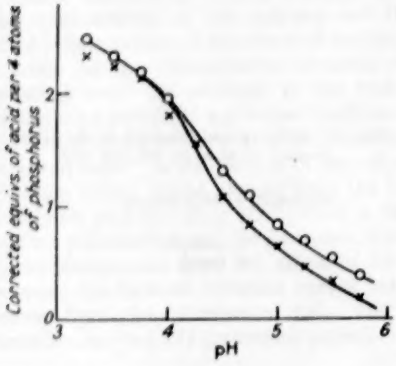


FIG. 4. *Titration curve of sodium deoxyribonucleate at zero concentration and ionic strength.*

× *Forward titration.* ○ *Backward titration.*

for the pG' values of the dissociating groups. The pG' values of the titrating groups at various concentrations and ionic strengths, and the calculated amount of secondary phosphoryl dissociation, are collected in Table 1.

The presence of a secondary phosphoryl dissociation was inferred by Gulland, Jordan, and Taylor [2] and by Lee and Peacocke [3] because of the necessity of introducing a small quantity of a group dissociating between pH 6 and 7 to explain their titration curves. This is also necessary to explain the present results. However, the forward titration curves (see Part VII) show no indication of the presence of such a group, and there is no evidence for a secondary phosphoryl dissociation from other sources. It cannot be considered definitely established that this group is a secondary phosphoryl dissociation. Lawley [4] has suggested that it may be due to an amino-dissociation modified by hydrogen bonding with primary phosphate groups. For 12 of the 13 backward titration curves analysed, the amount of this dissociation found was 0·19—0·21 equiv. per 4P atoms. This is less than that reported by Lee and Peacocke,[3] namely, 0·33 ± 0·07 equiv. for undried material calculated from the backward titration curve from pH 2, but is in agreement with the conclusions of Gulland, Jordan, and Taylor [2] who found 0·25 equiv., although it must be remembered that they employed incorrect analytical figures.

The Dissociation Constants.—The titration constants (pG') are evaluated by the equation $\mathrm{pH} = \mathrm{p}G' - \log [\beta/(1 - \beta)]$ where β is the degree of dissociation of the base concerned.

[2] Gulland, Jordan, and Taylor, *J.*, 1947, 1131.
[3] Lee and Peacocke, *J.*, 1951, 3361.
[4] Lawley, *Biochim. Biophys. Acta*, 1955, in the press.

Katchalsky, Shavit, and Eisenberg [5] have shown that the dissociation of a polymeric electrolyte may be represented by :

$$\mathrm{pH} = \mathrm{p}K_0 - \log \frac{\beta}{1-\beta} - \frac{0{\cdot}4343e\phi}{kT}$$

where ϕ is the electrostatic potential which may be evaluated from electrophoretic measurements. The term involving ϕ is not negligible for simple polyelectrolytes. A study of the electrophoretic mobility of sodium deoxyribonucleate has been made at various pH values and ionic strengths, and the magnitude of the term $\frac{0{\cdot}4343e\phi}{kT}$ has been calculated. It accounts correctly for the departure of the value of pG' from pK_0 at finite concentrations and ionic strengths (see Part IX, following paper).

TABLE 1. *Dissociation constants of sodium deoxyribonucleate at different concentrations and ionic strengths.*

Concn. of nucleate in equiv. 4P per l.	Ionic strength	pG'				Equiv. *sec.*-P(?) per 4P
		Guanine	Adenine	Cytosine	*sec.*-P(?)	
0	0	3·45	4·25	5·25	—	0·20
0·000113	—	3·35	4·20	5·25	6·45	0·21
0·000188	—	3·35	4·15	5·20	6·1	0·26
0·000281	—	2·95	3·90	5·10	6·2	0·20
0·000375	—	2·70	3·75	4·95	—	0·20
0·000750	—	2·50	3·70	4·90	6·1	0·19
0·001125	—	2·40	3·65	4·85	—	0·21
0·00142	0	2·60	4·05	5·25	5·90	0·21
,,	0·133	1·90	2·90	4·15	5·25	0·20
,,	0·255	1·70	2·60	4·05	5·10	0·20
,,	0·368	1·60	2·50	3·95	5·00	0·20
,,	0·492	1·50	2·50	3·95	4·75	0·20
,,	0·622	1·40	2·35	3·65	4·90	0·20
,,	0·748	<1·4	2·30	3·60	4·80	0·20
,,	0·871	<1·4	2·20	3·55	4·75	0·20

DISCUSSION

The values of pG' at zero concentration and ionic strength are the thermodynamic dissociation constants (pK) of the bases, and they are shown in the first line of Table 1. Increase in concentration and ionic strength both result in a smooth decrease in the pG' values, which becomes less marked at both high concentrations and high ionic strengths. The pG'–concentration curves however show an inflection at low concentrations not observed in the pG'–ionic strength curves. The effect of concentration is greatest on the pG' of guanine and less on the pG' of the groups titrating at higher pH, but the effect of ionic strength is least on the pG' of guanine.

Comparison of the Effects of Concentration and Ionic Strength.—Although concentration and ionic strength affect the pG' values in a similar manner, the ionic strength of the solution has a much greater effect on the pG' of the bases than has the concentration of nucleate, but the nucleate concentrations expressed in equivs. of 4P atoms per l., or as molar concentrations, are very small. For equal molar concentrations of nucleate and simple ion, the effect of the nucleate would be very much greater. Rough correspondence is shown between the ionic strength and the nucleate concentrations expressed as a percentage, but concentration has a relatively greater effect at low pH while ionic strength has the greater influence at higher pH. An attempt was made to estimate the " effective ionic strength " of sodium deoxyribonucleate at neutral pH, by titrating phosphoric acid in its presence. The titration curves over the neutral region, where the secondary phosphate groups are being titrated, were identical in the presence of and absence of 0·25% of sodium deoxyribonucleate, but small concentrations of added salt produced measurable differences. Clearly the nucleate exerts no measurable ionic-strength effect under these conditions and is less likely to do so at lower pH when its net charge is smaller.

[5] Katchalsky, Shavit, and Eisenberg, *J. Polymer Sci.*, 1954, **13**, 69.

Effect of Concentration and Ionic Strength on the Hysteresis.—The ionic strength of the solution has no effect on the alkaline hysteresis, measured by the area between the forward and the backward titration curves between pH 10 and 12 (Table 2). The acid hysteresis,

TABLE 2. *Effect of* KCl *on the alkaline hysteresis between* pH 10 *and* 12, *concn.* 0·25%.

Concn. of KCl (M)	0	0	0·1	0·25	1·00
Area of hysteresis (arbitrary scale)	47·5	46·2	47·0	48·5	46·5

as measured by the area berween the forward and the backward titration curves between pH 4 and 7, is directly proportional to the nucleate concentration (Fig. 5). Within experimental error, hysteresis always begins at pH 4·0, irrespective of the nucleate concentration. Clearly the forward and the backward titration curves are both influenced to the same extent by the ionic strength of the solution, and by the concentration of the nucleate. This suggests that hysteresis is not due to electrostatic forces, or to intermolecular interaction, but to some molecular property such as the intramolecular hydrogen bonding, to which it has already been ascribed.

The Charge carried by the Nucleate Ion.—The titration curves may be used to calculate the net negative charge borne by the nucleate ion. The calculations are strictly valid

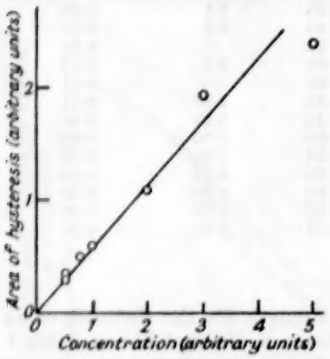


FIG. 5. *The effect of concentration on the hysteresis.*

only for a titration curve extrapolated to zero concentration and ionic strength [6] such as has been determined. The value of the charge so obtained will refer to a nucleate ion for which there has been no absorption of gegenions.

If $7·9 \times 10^6$ is taken for the molecular weight (Part VII), and 1231 for the molecular weight per 4P atoms, the maximum number of positive charges which are realisable when all the bases are titrated is 18,200. The number of positive charges on the nucleate ion has been calculated from the titration curve at zero concentration and ionic strength at various pH's and this is shown in Table 3. The net charge will be determined by the

TABLE 3. *Charge carried by the nucleate ion in the absence of gegenions.*

pH	3·0	3·5	4·0	4·5	5·0	5·5	6·0
No. of positive charges	15,100	13,600	11,200	6750	4240	2120	578
Net negative charge	10,580	12,080	14,480	18,930	21,449	23,560	25,102

number of positive charges, and by the number of negative charges carried by the primary phosphate groups. At pH values greater than 3 the primary phosphate groups may be considered to be fully dissociated and so the maximum negative charge is 25,680. The net negative charge on the nucleate ion is also shown in Table 3.

In practice at finite concentration and ionic strength, a number of Na^+ ions will be

[6] Abramson, Moyer, and Gorin, " Electrophoresis of Proteins," Reinhold Publ. Corpn., New York, 1942, pp. 156 *et seq.*

bound by ion-pair formation with the primary phosphate groups, and so the total negative charge is likely to be considerably less than 25,680; furthermore, Cl^- ions may form ion-pairs with the charged amino-groups, and so the total positive charge will also be less than that shown in Table 3. The change in the titration curves with concentration and ionic strength is to be ascribed partly to the influence of the bound gegenions on the electrostatic potential of the nucleate ion, as well as to the effect of the ionic strength on the activity coefficients. The net negative charge on the nucleate ion including its gegenions will therefore depend on the relative binding of the Na^+ and Cl^- gegenions, as well as on the degree of dissociation of the amino-groups. Values of the net negative charge calculated from the titration curves at various concentrations and ionic strengths, shown in Table 4, may allow for the effect on the activity coefficients of the simple ions, but take no account of the effect of absorption of the gegenions.

The figures in Table 4 may be compared with values of the net charge calculated by methods which allow for the contribution of the gegenions to it. For this sample of deoxyribonucleic acid, the value of the net negative charge calculated from electrophoretic mobility measurements (see Part IX, following paper) lies between 1500 and 2800, which is of the same order of magnitude as the values given by Creeth and Jordan [7] and Shack,

TABLE 4. *Net negative charge on the nucleate ion at various concentrations and ionic strengths, the contributions of the gegenions being disregarded.*

	Concn. 0·00142 equiv. of 4P per litre.						Absence of added salt		
pH	$\sqrt{I}$: 0	0·1	0·2	0·3	0·5	0·7	ε: 0·001125	0·000375	0·000281
6	25,420	—	—	—	—	—	25,680	25,680	25,360
5·5	23,880	24,780	25,420	—	—	—	24,530	24,390	23,940
5	21,830	23,240	24,010	24,650	25,490	—	22,920	22,600	22,080
4·5	19,310	20,730	22,080	23,120	24,070	24,720	20,930	20,480	19,010
4	15,440	17,980	19,110	20,540	21,960	22,920	18,500	17,910	16,680
3·5	12,780	14,580	15,680	17,050	18,580	19,560	15,800	15,280	13,930
3	—	—	—	—	14,080	15,480	13,480	12,180	10,880

Jenkins, and Thompsett.[8] It is thus evident that a large proportion of the charge of the nucleate ion itself is neutralised by the binding of gegenions of opposite charge.

The effects of concentration and of ionic strength on the net charge, the gegenions being disregarded, are similar, as shown by the figures in Table 4. This is to be expected from the similarity in the effects of concentration and ionic strength on the pG' of the bases.

Experimental.—The preparation and properties of the sodium deoxyribonucleate, the preparation of the solutions for titration, and the titration procedure were as in Part VII, except that in the experiments on the effect of ionic strength, solutions of the nucleate containing varying amounts of acid or alkali were titrated with concentrated lithium chloride solution.

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[*Received, July 15th*, 1955.]

[7] Creeth and Jordan, *J.*, 1949, 1409.
[8] Shack, Jenkins, and Thompsett, *J. Biol. Chem.*, 1952, **198**, 85.

31. *Electrophilic Substitution. Part I. Preliminary Investigations.*

By P. M. G. Bavin and M. J. S. Dewar.

This paper describes the first stages in a programme designed to provide quantitative data on the reactivity of aromatic systems in electrophilic substitutions. Preliminary investigations of the nitrations of phenanthrene, triphenylene, and pyrene are described. The work of Schmidt and Heinle [1] on the nitration of phenanthrene is criticised.

One of us [2] recently developed a simplified molecular-orbital (MO) treatment of chemical problems which seems to represent an advance over existing theories. Not only does it offer a complete justification for the qualitative electronic theory of organic chemistry which Lapworth, Robinson, Ingold, and others have developed, but it allows in principle simple quantitative estimates of the relations between structure and chemical reactivity. It is therefore a matter of some importance to test this aspect of the new theory, and we have initiated a programme designed to provide suitable quantitative data.

Since the treatment is based on the transition-state theory, it is necessary to select a reaction for which the transition state is likely to have a simple and known configuration. Aromatic substitution reactions form an obvious example, for it has been known [3] for some time that their rates can be interpreted in terms of a simple model for the transition state. The MO treatment can be applied most unambiguously to the reactions of hydrocarbons, and substitution in aromatic hydrocarbons is therefore a particularly suitable reaction; the more so since neither the classical electronic theory, nor the resonance theory, can predict the relative reactivities of different hydrocarbons, although they can be used (in a rather dubious manner) to estimate the relative reactivities of the different positions in a given hydrocarbon.

The treatment can be applied very simply to substitution in aromatic hydrocarbons, by using Wheland's model for the transition state. The activation energy ΔE should then be given [2] by :

$$\Delta E = C_x - 2\beta(a_{ot} + a_{om}) \equiv C_x - \beta N_t \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where C_x is a constant characteristic of the reagent X, β is the carbon–carbon resonance integral, and a_{ot}, a_{om} are the coefficients of the atomic orbitals of atoms adjacent to that (t) at which reaction takes place in the non-bonding molecular orbital of the transition state. The quantity $N_t \equiv 2(a_{ot} + a_{om})$ is therefore a direct measure of the relative reactivity of a given position in a given hydrocarbon, reactivity being greater the smaller N_t is. N_t may be termed the " reactivity number " of atom t. The coefficients can be found very simply, even in large polycyclic systems.

It has been shown [2,4] that the available evidence is in good general agreement with equation (1); in particular, since equation (1) holds regardless of the reagent, orientation in hydrocarbons should be the same for reagents of all types (electrophilic, nucleophilic, and radical); and this appears to be the case. A particularly striking confirmation is provided by recent measurements [5] of the relative rates of reaction of a wide range of hydrocarbons with methyl radicals. If it can be assumed that entropy effects are negligible, and that reaction occurs at one position in each hydrocarbon, it follows from equation (1) that

$$RT \log k/k_0 \equiv -\beta\,(N^\circ - N_t) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where k_0 is the velocity constant and N° reactivity number for substitution in benzene, and k and N_t the corresponding quantities for substitution at the most reactive position in some other hydrocarbon. The Table shows that the experimental results for methylation follow equation (2) closely. Strictly, one should correct the experimental results for

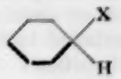
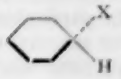
[1] Schmidt and Heinle, *Ber.*, 1911, **44**, 1448.
[2] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 2341 *et seq.*
[3] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.
[4] Bavin, Thesis, London, 1955.
[5] Levy and Szwarc, *J. Amer. Chem. Soc.*, 1955, **77**, 1949.

statistical factors, and the theoretical predictions for the fact that two or more positions in a hydrocarbon often have similar reactivity numbers; but these corrections would be small in comparison with the enormous range (10,000 : 1) of variation in the observed velocity constants. The rates of trichloromethylation of hydrocarbons by trichloromethyl radicals [6] must also follow equation (2), since Levy and Szwarc [5] have shown that the rates of methylation and trichloromethylation run parallel.

Comparison of observed and predicted reactivities for methylation of hydrocarbons.

Hydrocarbon	$\log k/k_0$	$N^\circ - N_t$	$(\log k/k_0)/(N_0 - N_m)$
Diphenyl	0·70	0·24	2·9
Naphthalene	1·34	0·50	2·7
Phenanthrene	1·43	0·51	2·8
Chrysene	1·76	0·64	2·8
Pyrene	2·10	0·80	2·6
Stilbene	2·26	0·80	2·8
Benzanthracene	2·67	0·96	2·8
Anthracene	2·91	1·04	2·8
Naphthacene	3·97	1·28	3·1

Although the new theory therefore seems to account quantitatively for the relative rates of radical substitution in hydrocarbons there is one disturbing feature. The value of the parameter β calculated from equation (2) and the data tabulated is too small (4·7 kcal., instead of ~20 kcal. required in calculations of conjugation energies). A similar difficulty has been known for some time to exist for naphthalene, where Wheland's calculations [3] implied that the α : β ratio in substitution should be very much greater than that observed. An obvious and likely explanation [7] would be that the structures (I) considered by Wheland are not transition states but stable intermediates; the transition states are of the type (II), where the reagent X is still remote and weakly bound.

(I)  (II) 

This would mean that the quantity ΔE in equation (1) is a heat of reaction and not an activation energy; and that the k's in equation (2) are equilibrium constants and not velocity constants. The success of the preceding treatment would then imply the existence of a linear relation between activation energy and heat of reaction—a common and familiar phenomenon.

Suppose that the energy of activation (ΔE) and the heat of reaction (ΔH) for substitution by a given reagent X are connected by such a linear relation, so that

$$\Delta E = A_x + B_x \Delta H \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where A_x and B_x are constants characteristic of X. Then equations (1) and (2) become :

$$\Delta E = A_x + B_x C_x - 2\beta B_x (a_{or} + a_{m}) = C_x' - 2\beta_x (a_{or} + a_{m}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$RT \log k/k_0 = -\beta_x (N^\circ - N_t) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where

$$\beta_x = \beta B_x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Therefore equation (2) will apply quite generally if the linear relation (3) holds, except in that β must now be regarded, not as a universal constant, but as a parameter characteristic of a given substitution reaction. As long as the reagent and the reaction conditions remain the same, β_x will remain constant; otherwise it may vary.

It is evident from equation (6) that, the smaller β_x is, the smaller will be the difference in reactivity between two different positions in a given hydrocarbon, and so the smaller the selectivity of orientation shown by the reagent X. This agrees well with the conclusions

[6] Kooyman and Farenhorst, *Trans. Faraday Soc.*, 1953, **49**, 58.
[7] Cf. Brown, *Quart. Rev.*, 1952, **6**, 63.

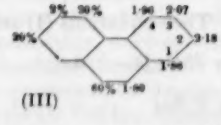
reached by Brown and his collaborators [8] concerning the selective effects of substituents on orientation; a highly reactive reagent will presumably be one for which β_x is small and such a reagent should show low selectivity. Their investigations show clearly the existence of linear relations between activation energies for substitution by different reagents and so provide indirect evidence for the relation indicated in equation (2). Brown and Nelson [9] expressed the view that transition states in electrophilic substitutions do not conform to the Wheland model, but involve less disturbance of the π-electrons in the substrate; our argument supports this view.

Although the available data on electrophilic substitution are in good general agreement with equation (2), there are some anomalies. Sulphonation and the Friedel–Crafts reaction commonly give " abnormal " products. In sulphonation these are known to arise only when the substitution becomes reversible, so that the proportions of isomers are determined by the thermodynamic equilibrium between them rather than by their rates of formation. The same is probably true of the Friedel–Crafts reaction.[10] Any valid test of equation (1) must be based on reactions which are definitely irreversible, such as nitration and halogenation.

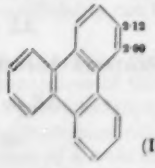
We have obtained evidence in support of Gore's [10] suggestion by showing that 9-acetylphenanthrene is the main product when phenanthrene is acetylated under conditions where the intermediate complex is precipitated and so removed from further reaction; acetylation under homogeneous conditions, in nitrobenzene, gives a mixture of the 2- and the 3-isomer.[11]

The nitration of phenanthrene does, however, seem to proceed in a manner very dissimilar to that predicted. Schmidt and Heinle [1] studied this reaction in great detail; they separated the mixture of mononitrophenanthrenes by laborious fractional crystallisation and reported that the proportions of isomers were those shown in (III). These are in qualitative disagreement with the relative reactivities predicted from the reactivity numbers [also shown in (III)]. In particular, they stated that they could find no trace of the 1-isomer, despite a careful search; the 1-position is predicted to be second in order of reactivity, and to be only a little less reactive than the 9-position.

We have re-examined the nitration of phenanthrene in hot acetic acid, following the procedure of Schmidt and Heinle. The product was a dark uncrystallisable gum and contained large quantities of coloured materials strongly adsorbed on alumina (probably quinones and polynitro-compounds). It is therefore evident that the percentage composition given by Schmidt and Heinle must have been based on the total weight of pure isomers isolated and not on the weight of the crude product; since the separation of these isomers, even by chromatography, is exceedingly difficult, the yields of pure isomers



(III)



(IV)

obtained by them by simple fractional crystallisation were probably small. Further, the identities of the materials described by them as 2- and 4-nitrophenanthrene are in doubt; [12] their materials were at best impure and may even have been mixtures or solid solutions containing little of the isomers claimed. Schmidt and Heinle's results cannot therefore be regarded as reliable, or as evidence against the order of reactivities predicted theoretically.

We have nitrated phenanthrene, using a large excess of the hydrocarbon in acetic anhydride and working at low temperatures. Under these conditions the product is a yellow crystalline mixture of mononitrophenanthrenes, containing only traces of quinones

[8] Brown and co-workers, *J. Amer. Chem. Soc.*, 1955, **77**, 2300, 2306, 2310, 3037.
[9] Brown and Nelson, *ibid.*, 1953, **75**, 6592.
[10] Gore, personal communication; cf. *Chem. Rev.*, 1955, **55**, 229.
[11] Mosettig and van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704.
[12] Bavin and Dewar, *J.*, 1955, 4477.

or polynitro-compounds. Chromatography proved unsuccessful for quantitative separation, but we were able to isolate 1-nitrophenanthrene for the first time.[13] We were at first misled as to the proportion of this isomer in the mixture, believing it to be very small; subsequent examination has indicated that it is in fact a major component. This has been confirmed by Mr. E. W. T. Warford (unpublished work) who has shown by isotope dilution analysis that it forms almost one-third of the nitration product.

We have also studied the nitration of triphenylene. The only information in the literature concerning orientation referred to Friedel–Crafts reactions and sulphonation, which give 2-substitution, whereas the reactivity numbers shown in (IV) indicate that the 1-position should be somewhat the more reactive. Nitration of triphenylene, under the conditions used for phenanthrene, gave almost exclusively a mixture of mononitrotriphenylenes; previously only a trinitrotriphenylene, of unknown structure, had been described.[14] The mixture of 1- and 2-nitrotriphenylene, m. p. 169° and m. p. 165—166°, respectively, was separated by chromatography. These were oriented by reduction to the aminotriphenylenes and conversion into the two fluorotriphenylenes. Authentic 2-aminotriphenylene was prepared from 2-acetyltriphenylene[15] by Beckmann rearrangement of the oxime to 2-acetamidotriphenylene followed by hydrolysis. Authentic 2-fluorotriphenylene was prepared by the Rapson synthesis[16] from *p*-bromofluorobenzene and *cyclo*hexenyl*cyclo*hexane. The ratio of isomers in the nitration product is estimated to be 1·0 : 1·0 ± 0·1.

Since substitution in the 1-position of triphenylene must be subject to severe steric hindrance, this result implies that the 1-position is intrinsically the more reactive, as predicted.

In nitration of pyrene under similar conditions we find that 1-nitropyrene is almost the sole product; no evidence could be found for the formation of any other mononitropyrene. This is surprising, for although the 1-position should be the most reactive, the difference between the reactivity numbers for 1- and 4-substitution is less than that between the numbers for α- and β-substitution in naphthalene, where the ratio of isomers formed on nitration is only * about 10 : 1. We are confident that the ratio is very much greater than this in the case of pyrene.

In conclusion, we have shown that nitration of aromatic hydrocarbons proceeds cleanly under suitable conditions, giving almost exclusively mixtures of mononitro-derivatives; it is therefore an ideal reaction for quantitative studies of reactivity. We have also shown that previous work on the nitration of phenanthrene is unreliable and that there is no evidence that the predictions of molecular-orbital theory in this case are incorrect; and we have shown that the nitration of triphenylene conforms qualitatively with prediction.

Experimental

Purification of Phenanthrene.—Phenanthrene was purified by boiling with maleic anhydride in xylene, followed by crystallisation from acetic acid. It formed colourless plates, m. p. 100° (lit., 100°), and the absorption spectrum was identical with that reported.[18]

Nitration of Phenanthrene.—(*a*) Nitration of phenanthrene by the method of Schmidt and Heinle,[1] with a slight excess of nitric acid in hot glacial acetic acid, gave a dark resin which appeared to contain large quantities of oxidation and polynitration products. (*b*) Phenanthrene (5 g.) in acetic anhydride (100 ml.) was treated at 10° with a solution of fuming nitric acid (0·25 equiv.) in acetic anhydride (4 ml.). Next day the yellow solution was poured into dilute sulphuric acid and crushed ice, and organic material extracted with benzene (5 × 100 ml.). After being washed with water, sodium carbonate solution, and again water, the solution was

* Fierz-David and Sponagel[17] report a ratio of 20 : 1; we have, in a preliminary investigation, found values in the range 11—16 : 1.

[13] *Idem, Chem. and Ind.*, 1953, 543.
[14] Mannich, *Ber.*, 1907, **40**, 160.
[15] Buu-Hoï and Jacquignon, *J.*, 1953, 941.
[16] Rapson, *J.*, 1941, 15.
[17] Fierz-David and Sponagel, *Helv. Chim. Acta*, 1943, **26**, 98.
[18] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley and Sons, New York, 1941, No. 341.

evaporated, and the residue chromatographed from light petroleum on alumina (6 × 50 cm.). Phenanthrene (4·2 g.) was eluted in the first 15 l. After 250 l. of eluant had passed through the column, elution was continued with light petroleum containing benzene (2%), and fractions (500 ml. each) were collected. Most of the recovered materials melted over wide ranges and pure isomers were isolated only in a few cases. The isomers when isolated were identified by mixed m. p.s and ultraviolet absorption spectra with synthetic specimens.[12] Fraction 5 on recrystallisation first from methanol, then from acetic acid, gave 3-nitrophenanthrene, m. p. 173—174°. Fraction 6 also gave 3-nitrophenanthrene; recrystallisation (from light petroleum) of the material contained in the mother-liquors gave 1-nitrophenanthrene, m. p. 133—134°. Fraction 12 on recrystallisation from light petroleum gave 1-nitrophenanthrene; 9-nitrophenanthrene, m. p. 116°, was isolated from the mother-liquors by crystallisation from acetic acid. Fractions 13—21 consisted mainly of 9-nitrophenanthrene, m. p. 114—116° after recrystallisation from acetic acid. Fraction 22 after several crystallisations from methanol had m. p. 114—116°, strongly depressed by 9-nitrophenanthrene, scarcely depressed by 2-nitrophenanthrene; the ultraviolet absorption spectrum resembled that of 2-nitrophenanthrene.

It appears that 1- and 9-nitrophenanthrene are major components, the former appearing in fractions 5—12, the latter in fractions 12—21, also that quantitative separation of the mixture by chromatography would present a very difficult problem.

Acetylation of Phenanthrene.—A solution of pure phenanthrene (20 g.) in carbon disulphide (150 ml.) was cooled to 0°. Freshly distilled acetyl chloride (12·2 g., 1·4 mol.) was then added, followed by powdered aluminium chloride (35 g.). After ½ hour's stirring at 0° the mixture was left overnight at room temperature. Next day the complex was decomposed with ice and hydrochloric acid, the carbon disulphide distilled off, and the residual red oil isolated with carbon tetrachloride and fractionated. Mixed acetylphenanthrenes (16 g.) were collected at 260—280°/15 mm. Crystallisation from methanol containing a little acetone gave 2-acetylphenanthrene (0·35 g.), m. p. and mixed m. p. 140—142°. The hot mother-liquors were diluted with an equal volume of hot water and gave sticky needles, m. p. 60—70°, depressed by 3-acetylphenanthrene. Oxidation of this crude material (A) with hypochlorite gave an acid which was esterified in chloroform with diazomethane; after chromatography from light petroleum on alumina the methyl ester crystallised from light petroleum in colourless needles, m. p. 114—115°, undepressed by methyl 9-phenanthroate.[19] The yield of ester, based on (A), was 74%; (A) was therefore impure 9-acetylphenanthrene.

Nitration of Triphenylene.—Triphenylene [16] was purified by chromatography from light petroleum on alumina followed by crystallisation from benzene; it had m. p. 198—199°. Purified triphenylene (12 g.) in acetic anhydride (1500 ml.) was nitrated at 25° with acetyl nitrate (0·5 mol.). Next day the solution was poured into crushed ice and dilute sulphuric acid, and the product isolated with chloroform and chromatographed from light petroleum on alumina. After all the unchanged triphenylene (5·1 g.) had been eluted, elution was continued with light petroleum–benzene (5 : 1), giving a mixture of mononitrotriphenylenes (6·68 g.). Only traces of other materials remained on the column. The mixed mononitrotriphenylenes were rechromatographed and fractions collected : fraction 1, trace of triphenylene; fractions 2—6 (A), yellow prisms, m. p. 164—169° (2·91 g.); fraction 7, poorly formed crystals, m. p. 140—151° (0·52 g.); fractions 8—11 (B_1), yellow needles, m. p. 162—165° (1·12 g.); fractions 12—19 (B_2), yellow needles, m. p. 148—164° (1·9 g.). Crystallisation of fractions (A) from toluene gave yellow prisms, m. p. 169°, of *1-nitrotriphenylene* (Found : C, 79·3; H, 4·1; N, 4·9. $C_{18}H_{11}O_2N$ requires C, 79·1; H, 4·1; N, 5·1%). Crystallisation of fractions (B_1) from toluene and then from acetic acid gave pale yellow needles, m. p. 165—166°, of *2-nitrotriphenylene* (Found : C, 79·0; H, 4·2; N, 5·2%). Fraction (7) was shown by thermal analysis to be a mixture of about 60% of 1- and 40% of 2-nitrotriphenylene. Fractions (B_2) were shown by recrystallisation to be essentially impure 2-nitronaphthylamine.

1-*Aminotriphenylene.*—Reduction of 1-nitrotriphenylene (0·4 g.) with hydrazine and Raney nickel gave 1-*aminotriphenylene*, yellow needles (from toluene), m. p. 104—105° (Found : C, 88·2; H, 5·45; N, 5·75. $C_{18}H_{13}N$ requires C, 88·9; H, 5·4; N, 5·8%), not identical with 2-aminotriphenylene. The *N-acetyl derivative* crystallised from toluene in colourless needles, m. p. 252° (Found : N, 4·9. $C_{20}H_{15}ON$ requires N, 4·9%). The *benzylidene derivative* crystallised from alcohol in pale yellow needles, m. p. 140—140·5° (Found : N, 4·2. $C_{25}H_{17}N$ requires N, 4·2%). Solutions of the amine in hydrocarbon solvents showed an intense fluorescence.

[19] Pschorr, *Ber.*, 1896, **29**, 496.

1-*Fluorotriphenylene*.—The nitro-compound (1·4 g.) was reduced and the crude amine diazotised and converted into the diazonium fluoroborate. This was decomposed by boiling it for 30 min. in light petroleum (b. p. 100—120°), and the resulting solution chromatographed on alumina. The highly fluorescent 1-*fluorotriphenylene* was eluted first, and crystallised from toluene in yellowish needles, m. p. 173—174°, raised by vacuum-sublimation and recrystallisation to 174—175° (Found: C, 87·9; H, 4·7. $C_{18}H_{11}F$ requires C, 87·8; H, 4·5%). The compound was shown to differ from 2-fluorotriphenylene, by mixed m. p. and comparison of the spectra.

1-p-*Fluorophenyl*-2-cyclo*hexenyl*cyclo*hexanol*.—To a Grignard reagent prepared from *p*-bromofluorobenzene (87·5 g.) and magnesium (13·5 g.) was added slowly 2-*cyclo*hexenyl*cyclo*hexanone (90 g.), and the solution was left overnight. Isolation of the *alcohol* in the usual way gave an oil (79 g., 58%), b. p. 160—164°/1·5 mm., $n_D^{20\cdot5}$ 1·5400, which solidified and then crystallised from light petroleum in prisms, m. p. 42—45° (Found: C, 79·1; H, 8·4. $C_{18}H_{23}OF$ requires C, 78·8; H, 8·4%).

2-*Fluoro*-5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-*octahydrotriphenylene*.—The alcohol (32·5 g.) in carbon disulphide (100 ml.) was added to a suspension of powdered aluminium chloride (32 g.) in carbon disulphide (100 ml.) at 0°. After 1 hr. the mixture was left at room temperature. Next day water was added and the hydrocarbon isolated through its picrate (orange needles, m. p. 180°, from benzene or alcohol). After decomposition of the picrate with alumina in the usual way, 2-*fluoro-octahydrotriphenylene* was obtained as a white solid which crystallised from alcohol in needles, m. p. 146—147° (Found: C, 84·8; H, 7·5. $C_{18}H_{19}F$ requires C, 85·0; H, 7·5%).

2-*Fluorotriphenylene*.—Dehydrogenation of the octahydro-derivative over palladised charcoal at 310—335° gave 2-*fluorotriphenylene*, in almost theoretical yield, crystallising from light petroleum in colourless needles, m. p. 185—185·5° (Found: C, 88·3; H, 4·8%).

2-*Acetamidotriphenylene*.—2-Acetyltriphenylene [15] (1·6 g.) was converted into its oxime with hydroxylamine hydrochloride (1 g.) in pyridine (5 ml.) and ethanol (7 ml.), and the crude oxime (m. p. 190—196°) treated with phosphorus pentachloride (1·2 g.) in benzene (30 ml.), then boiled under reflux for 15 min. Water was added and the *acetamidotriphenylene* collected; it crystallised from methanol in colourless needles (0·7 g.), m. p. 260—261° (Found: C, 84·0; H, 5·4; N, 5·05. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3; N, 4·9%).

2-*Aminotriphenylene*.—The acetyl derivative (300 mg.) was boiled under reflux for 36 hr. with hydrochloric acid (5 ml.) in ethanol (200 ml.). The *amine*, isolated by evaporation and basification, crystallised from light petroleum in pale yellow blades, m. p. 139—140° (Found: C, 89·0; H, 5·7; N, 5·9. $C_{18}H_{13}N$ requires C, 88·9; H, 5·4; N, 5·8%).

Orientation of 2-*Nitrotriphenylene*.—Reduction of 2-nitrotriphenylene with hydrazine and Raney nickel gave 2-aminotriphenylene, crystallising from light petroleum in colourless blades, m. p. and mixed m. p. 142—143°. The amine was converted, as for the 1-isomer, into 2-fluorotriphenylene which crystallised from toluene in needles, m. p. 181—182°, raised to 182—183° by recrystallisation from light petroleum, mixed m. p. with synthetic 2-fluorotriphenylene 184—185°.

Nitration of Pyrene.—Pyrene was purified by chromatography from benzene–light petroleum (1 : 1) on alumina, forming rhombohedral plates, m. p. 153—154° (lit., 156°). Pure pyrene (10 g.) in acetic anhydride (250 ml.) was nitrated at room temperature with a solution of 95% nitric acid (2 ml.) in acetic anhydride (3 ml.). Next day the solution was poured into dilute sulphuric acid and crushed ice, and the precipitate recrystallised from methanol and then from acetic acid, giving orange-yellow needles (5·1 g.) of 1-nitropyrene, m. p. 155° (lit., 153—154°). Concentration of the mother-liquors gave a further 2·9 g., m. p. 146—148°. Dilution of the filtrate with water gave a solid (1·9 g.) which was chromatographed from light petroleum on alumina. After a trace of pyrene, more 1-nitropyrene was collected (1·2 g.); the remaining material, which was highly coloured and strongly adsorbed, probably consisted of dinitropyrenes. Repeated chromatography failed to yield any isomers in the 1-nitropyrene fractions.

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32. *The Kinetics of the Alkaline Hydrolysis of Esters and Amides of 1- and 2-Naphthoic Acid.*

By P. Fitzgerald, J. Packer, J. Vaughan, and A. F. Wilson.

The kinetics of alkaline hydrolysis, in alcohol–water solvents, of the methyl and ethyl esters of 1- and 2-naphthoic acid have been followed in the temperature range 30—60°. The order of reactivity found for the methyl esters is the reverse of that found by Bergmann and Hirshberg,[1] working with methanolic potassium hydroxide, and the order now found agrees with results for ethyl esters and with results here reported for the corresponding naphthamides at 70—80°. The relative rates of hydrolysis of ethyl and methyl esters for a given naphthoic acid are discussed and a value is derived, from results on ethyl 2-naphthoate, for the Hammett σ constant for the fused benzene ring.

In accord with calculations showing that electron density at $C_{(1)}$ of naphthalene is greater than that at $C_{(2)}$,[2] reaction of naphthalene with electrophilic reagents occurs predominantly at position 1, provided that it is not complicated by exceptionally strong temperature- and solvent-dependence (as in, *e.g.*, sulphonation, Friedel–Crafts alkylation). The evidence concerning nucleophilic attack is, however, neither extensive nor unambiguous.

Few reactions involving nucleophilic displacement of groups at either position 1 or position 2 have been carried out and evidence for order of relative reactivity is inconclusive.[3] But the difference in electron density should be reflected in the relative reactivities of suitable side chains, and reactions of such derivatives may be chosen which are more amenable to kinetic study than are reactions involving direct substitution in the ring. In such reactions which have been investigated, it is possible to link greater reactivity of the 1-naphthyl compound (*e.g.*, neutral hydrolysis of bromomethylnaphthalenes [4]) with a preliminary rate-determining ionisation which would be aided by electron-donating groups, whilst greater reactivity of the 2-naphthyl compound (*e.g.*, acid hydrolysis of naphthalenesulphonyl chlorides [5]) may be associated with an S_N2 type mechanism in which the rate-determining step is attack by the nucleophilic agent. Such interpretations are compatible with calculated electron densities, but of special interest, however, are the results of Bergmann and Hirschberg [1] who determined the second-order rate constants for the alkaline hydrolysis of methyl 1- and 2-naphthoates in methanol at 60°. Hydrolysis of the 1-naphthoate was observed to occur at the higher rate (*ca.* 4 : 3). It is difficult to interpret these results, especially on the basis of a $B_{AC}2$ mechanism by which, it may be assumed, these reactions occur. In view of the greater electron-donating capacity of the 1-naphthyl group it would be expected, *a priori*, that methyl 2-naphthoate would undergo hydrolysis more rapidly than the 1-ester.

The alkaline hydrolysis of the two methyl naphthoates in methanol–water has been investigated by us and the results, together with those of similar hydrolytic studies on the ethyl esters in ethanol–water and on the corresponding amides in dioxan–water, are now reported.

Experimental

Materials.—1- and 2-Naphthoic acid melted at 160° and 182° respectively. The esters were prepared by using the purified alcohols and dry hydrogen chloride. Methyl 2-naphthoate melted at 76°. B. p.s of the other three esters were: ethyl 1-, 194—196°/45 mm., and 2-naphthoate, 194—195°/37 mm.; methyl 1-naphthoate, 165—166°/17 mm., m. p. 36°. 1-Naphthamide melted at 207° and 2-naphthamide at 196—196·5°. Solvents were purified by standard methods, the alcohols being aldehyde-free (Schiff's reagent), and sodium hydroxide

[1] Bergmann and Hirshberg, *J.*, 1936, 331.
[2] Jaffé, *J. Chem. Phys.*, 1952, **20**, 778.
[3] Cf., *inter al.*, Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273; also ref. 2.
[4] Ingold and Patel, *J. Indian Chem. Soc.*, 1930, **7**, 95.
[5] Linetskaya and Sapezhorikova, *Zhur. prikład. Khim.*, 1948, **21**, 876.

solutions being free from carbonate. The temperature of the thermostat bath was maintained within ±0·02°.

Ester Hydrolyses.—The kinetic procedure was similar to that used by Evans, Gordon, and Watson.[6] The esters were hydrolysed in aqueous alcohol (85% of alcohol by wt.), the alcohol used being that corresponding to the alkyl group of the ester under study. Boiled-out distilled water was used and aliquots for analysis were kept under nitrogen. Amounts of ester and sodium hydroxide initially used were equivalent, and the simplified form $k = x/[ta(a - x)]$ of the second-order rate equation was found to apply in all instances (see Appendix). The minimum number of runs carried out under any chosen conditions was 2 and the average was 3—4. Runs with unequal concentrations of ester and alkali acted as a check on the assumed rate-dependence. Kinetics were followed at four temperatures and results of all runs are given in the Table. The mean values for rate constants led to satisfactory Arrhenius plots of log k *versus* $1/T$ and values for the activation energy (E) and the temperature-independent term ($\log_{10} B$) are included in the Table.

	10^3k (l. mole^{-1} sec.$^{-1}$)						E (kcal.)	$\log_{10} B$
Ethyl esters in 85% ethanol–water (w/w)								
	30°		40°	50°	60°			
1-Naphthoate	0·68,	0·63, 0·59	1·67, 1·60, 1·57, 1·70, 1·50	2·63, 2·67, 3·10, 3·10	5·8, 5·9, 5·9		14·5	7·3
2-Naphthoate	1·50,	1·63, 1·61, 1·54	3·52, 3·58, 3·47, 3·77, 3·66	8·0, 8·3, 8·3	17·3, 17·5, 17·3		16·1	8·8
Methyl esters in 85% methanol–water (w/w)								
1-Naphthoate	0·152,	0·152, 0·148	0·52, 0·48, 0·50	1·22, 1·24	2·48, 2·45, 2·50		18·7	9·7
2-Naphthoate	0·36, 0·35,	0·33, 0·38, 0·37	0·97, 0·87, 0·96, 0·83, 0·96, 0·93	2·65, 2·66	6·5, 6·4, 6·5		19·4	10·5
Naphthamides in 20% dioxan–water (v/v)								
	70°		80°					
1-Naphthamide	0·0103		0·0236	—	—		20·0	7·7
2-Naphthamide	0·146		0·253	—	—		13·3	4·6

Amide Hydrolyses.—The reaction vessels used and the methods of analysis followed have been described.[7,8] The analytical procedure was checked for the solvent (20% dioxan–water, v/v) and no interference could be detected. With 2-naphthamide the extent of reaction with hypobromite was sufficiently small to allow use of direct titration after correction for the slight amide–hypobromite reaction. With 1-naphthamide, the interaction with hypobromite was extensive and the distillation procedure was used with satisfactory results. The molar ratio of alkali : amide was >100 : 1 in every run and the kinetics were of the first order with respect to amide. Variation of amide concentration confirmed the expected pseudounimolecular kinetics. Kinetics were followed at 70° and 80° and at each temperature rates were measured at five different alkali concentrations (0·4—1·6M for 1-naphthamide and 0·15—0·65M for 2-naphthamide). Duplicate runs showed agreement as good as that previously reported for aliphatic amides.[8] For each amide, when k_1 (first-order rate constant) was plotted against [NaOH], the resulting graph was linear, the slope k being the second-order rate constant for the reaction. Values for k, E, and $\log_{10} B$ are in the Table.

Discussion

Comparison of the present results for methyl esters with those of Bergmann and Hirshberg [1] shows a difference in absolute values, and the order of reactivity now found is the reverse of that indicated by them. The earlier, much lower values are understandable in the light of the solvent used, which appears to have been almost 100% methanol, in which hydroxyl-ion concentration is extremely low (see below). The difference in order, on the other hand, is difficult to accept without the arbitrary assumption of a reversal in order within the range 85—100% methanol. In estimating the importance of the discrepancy, however, it must be borne in mind that Bergmann and Hirshberg's figures

[6] Evans, Gordon, and Watson, *J.*, 1937, 1430.
[7] Ivory, McKenzie, and Vaughan, *J.*, 1952, 3264.
[8] Packer, Thomson, and Vaughan, *J.*, 1955, 2601.

are the result of kinetic work at one temperature and appear to be derived from single runs followed only for a very small degree of hydrolysis; furthermore Bergmann and Hirshberg used the simplified form of the second-order rate equation, which appears not to be applicable in nearly absolute methanolic sodium hydroxide. The order of reactivity now reported finds a parallel in the results on the ethyl esters, and similar work on the corresponding amides also shows the same relative rate order. Unexpectedly, in the ester hydrolyses the slower reaction (that of the 1-naphthoates) has the smaller Arrhenius energy of activation although in the amide hydrolyses the slower reaction (again that of the 1-derivative) has the higher energy of activation. There appears to be no obvious explanation of this difference; the results do suggest, however, that there may be no simple correlation between electron density and Arrhenius energy of activation in the naphthalene series.

Our results on ester hydrolysis also serve for a comparison of the reaction rates of methyl and ethyl esters of a given naphthoic acid. At any one temperature the rate constant for ethyl 1- or 2-naphthoate in 85% ethanol is higher than that for methyl 1- or 2-naphthoate respectively in 85% methanol. Bearing in mind the assumed mechanism for such ester hydrolysis it would be expected that, had the reactions been carried out in the same solvent, the more highly positive-inductive ethyl group should lead to a comparatively slower reaction for the ethyl ester. Ingold,[9] for example, found this effect in the hydrolyses of methyl and ethyl acetate. Comparison of rate constants obtained in different solvents is clearly complicated by many factors but in the present case a major effect, tending to favour faster reaction of the ethyl ester, can be discerned. Caldin and Long [10] studied the replacement, at 25°, of hydroxide ion by ethoxide ion in solutions made by dissolving sodium or sodium hydroxide in ethanol–water mixtures. It is clear, from their measurement of equilibrium constants, that ethoxide-ion concentration in 85% ethanol at 25° is high (*ca.* 60% total base).

A somewhat similar relation, with a different equilibrium constant, is likely to hold for hydroxide ions in methanol. Woodland, Carlin, and Warner [11] demonstrated the greater acidity of methanol than of water, and Hine and Hine [12] have given the values for the relative acidities of ethanol, methanol, and water in propan-2-ol solution as 0·95, 4·0, and 1·2 respectively. Clearly, addition of equal amounts of alkali to methanol and ethanol leads to a higher concentration of *hydroxide* ions in ethanol than in methanol. Because attack by methoxide ion on the methyl ester merely produces another ester molecule, the lower hydroxide-ion concentration in the methanolic solution results in a lower rate of hydrolysis than might be expected from the amount of sodium hydroxide introduced. The extent of such lowering of rate would be less in the corresponding case of ethanol and ethyl ester. From the experimental figures on relative rates, it appears possible that this factor is much more important than the difference in inductive effects displayed by the alkyl groups concerned. Other factors, such as difference in dielectric constant of the medium, will doubtless play their parts.

From the present results on ethyl 2-naphthoate a value may be obtained for the Hammett σ constant of the fused benzene ring in the 2-naphthyl derivative. Calculations were based on Jaffé's equation,[13] and rate constants were taken from the Arrhenius plot to obtain figures for σ at temperatures for which other data are available. The relevant values, together with the probable errors, are $\sigma_{25} = 0{\cdot}079 \pm 0{\cdot}017$, $\sigma_{35} = 0{\cdot}055 \pm 0{\cdot}021$, $\sigma_{50} = 0{\cdot}051 \pm 0{\cdot}019$. Two values have previously been reported. Hammett [14] gives $\sigma_{25} = 0{\cdot}170 \pm 0{\cdot}10$ and Price and Michel [15] give $\sigma_{25} = 0{\cdot}019$. In checking the calculation of the latter workers, we obtained 0·001, although recalculation of other σ constants given in the same paper confirmed the values quoted.

[9] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953, p. 758.
[10] Caldin and Long, *J.*, 1954, 3737.
[11] Woodland, Carlin, and Warner, *J. Amer. Chem. Soc.*, 1953, **75**, 5835.
[12] Hine and Hine, *ibid.*, 1952, **74**, 5266.
[13] Jaffé, *Chem. Rev.*, 1953, **53**, 254.
[14] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188.
[15] Price and Michel, *J. Amer. Chem. Soc.*, 1952, **74**, 3653.

Appendix

In our system for ester hydrolysis the concentrations of alcohol and water change by negligible amounts and the ionic strength remains constant. The equilibrium constant (K) for the equation $OH^- + EtOH \rightleftharpoons H_2O + EtO^-$ may be written as $[H_2O][EtO^-]/[OH^-][EtOH]$. The linear plots which occur owing to the use of the simplified form of the second-order rate equation arise from the proportionality between the amount of hydroxide ion and the total amount of base present (hydroxide and ethoxide ions). It will be seen from the expression for K that this will only be true if changes in $[H_2O]$ and [EtOH] are negligible. Use of 85% ethanol–water is satisfactory in this respect but it appears that in a solvent of very high alcohol concentration (*e.g.*, >99%) and with base concentration greater than, say, 0·01M some drift from linearity of plots might be expected. The general argument appears true for use of both ethanol and methanol, which give rise to values of K which, while different numerically, are of the same order of magnitdue. Further, for alcohol–water systems to which the simple second-order equation is applicable the derived rate constant, k, is not the same as that which would be obtained from the unsimplified form with knowledge of the actual hydroxide-ion concentration. It is readily demonstrable that the relation, which in theory should hold between the two rate constants, is $k = k_{true} \cdot s/(1 + s)$ where $s = [OH^-]/[EtO^-]$. Provided that the mixed solvent remains the same, however, k values found by use of the simple equation are fully adequate for the main purpose of such measurements, *i.e.*, the comparison of rates.

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33. *Perfluoroalkyl Derivatives of Sulphur. Part IV.* Perfluoroalkanesulphonic Acids.*

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Electrolysis of methanesulphonyl fluoride or chloride in anhydrous hydrogen fluoride yields trifluoromethanesulphonyl fluoride almost quantitatively. The conversion of the last compound into $CF_3 \cdot SO_2X$ (X = NH_2, NEt_2, OMe, and OEt) and $CF_3 \cdot SO_3M$ (M = K, Na, Ag, and ½Ba) is described.

The infrared spectra of compounds which contain $-SO_2^-$ and $-SO_3^-$ groups are considered.

Trifluoromethanesulphonic acid was first prepared by the route :

$$CS_2 \xrightarrow{IF_5} CF_3 \cdot S_4 \cdot CF_3 \xrightarrow[h\nu]{Hg} (CF_3 \cdot S)_2Hg \xrightarrow{H_2O_2} CF_3 \cdot SO_3H$$

and shown to be a very strong acid by conductivity measurements in aqueous and acetic acid solutions.[1] An alternative route from bistrifluoromethyl disulphide was described in Part II :[2]

$$CF_3 \cdot S \cdot S \cdot CF_3 \xrightarrow[h\nu]{Cl_2} CF_3 \cdot SCl \xrightarrow{H_2O_2} CF_3 \cdot SO_2Cl \xrightarrow{Cl_2 - H_2O} CF_3 \cdot SO_3H$$

Although both these routes are potentially capable of extension to other perfluoroalkanesulphonic acids by use of disulphides prepared by the general reaction of perfluoroalkyl iodides with sulphur,[3] they suffer from the disadvantage that photochemical homolytic fission of the disulphide bond is slow. It was shown earlier[4] that perfluoroalkyl sulphur

* Part III, *J.*, 1955, 3871.

[1] Haszeldine and Kidd, *J.*, 1954, 4228 (Part I); Haszeldine, *Angew. Chem.*, 1954, **66**, 693; Amer. Chem. Soc. Meetings, Chicago, 1953, and New York, 1954.

[2] Part II, Haszeldine and Kidd, *J.*, 1953, 2901.

[3] Haszeldine *et al.*, *J.*, 1952, 2198, 2549; 1953, 3219.

[4] Clifford, El-Shamy, Emeléus, and Haszeldine, *J.*, 1953, 2372.

compounds could be prepared by electrolysis of a solution of dimethyl sulphide or of carbon disulphide in anhydrous hydrogen fluoride, and a similar approach has now proved successful and given a convenient general route to perfluoroalkanesulphonic acids $CF_3{\cdot}[CF_2]_n{\cdot}SO_3H$. The present communication illustrates this for trifluoromethanesulphonic acid. It has been stated recently [5] that perfluoroalkanesulphonic acids have been prepared, but no details of technique, yield, or product have yet appeared.

Electrolysis of a solution of methanesulphonic acid in anhydrous hydrogen fluoride produces oxygen difluoride which, despite attempts to remove it in the absorption train, causes violent explosions which shatter parts of the apparatus. That production of oxygen difluoride is associated with the hydroxyl group of methanesulphonic acid, probably arising from water formed during fluorination of the acid, is shown by the fact that electrolysis of methanesulphonyl fluoride in anhydrous hydrogen fluoride proceeds smoothly and rapidly to give trifluoromethanesulphonyl fluoride in 96% yield. Methane sulphonyl fluoride was prepared for this purpose in high yield by reaction of the chloride with aqueous potassium hydrogen difluoride:

$$CH_3{\cdot}SO_3H \longrightarrow CH_3{\cdot}SO_2Cl \xrightarrow[KHF_2]{\text{Aq.}} CH_3{\cdot}SO_2F \xrightarrow[\text{in HF}]{\text{Electrol.}} CF_3{\cdot}SO_2F$$

Trifluoromethanesulphonyl fluoride (b. p. −21·7°) is swept out of the electrolysis cell by the hydrogen also produced, and the only by-products detected are fluoroform (1%) and carbon tetrafluoride.

The synthesis can be simplified still further by use of methanesulphonyl chloride rather than the fluoride, since electrolysis of this compound is also easily controlled and gives high yields of trifluoromethanesulphonyl fluoride; hydrogen chloride appears as additional product. The above reactions are of general application and make perfluoroalkanesulphonic acids available in quantity; subsequent communications will describe some of the properties of these extremely strong, surface-active acids.

The conductivity of methanesulphonyl chloride or fluoride in anhydrous hydrogen fluoride is doubtless due to formation of $CH_3{\cdot}\overset{+}{S}(:O)(OH)F$ and F^- ions. Electrolysis of the solution causes migration of the (solvated) fluoride ion to the anode where its discharge could be followed by one or both of two reactions. It could react with methanesulphonyl fluoride, adsorbed through the $-SO_2-$ group, on the surface of the anode. This does not mean that free fluorine atoms are necessarily produced, since a surface reaction could occur. Alternatively, discharge of fluoride could lead to formation of a higher fluoride of nickel containing ter- or quadri-valent nickel. If formed, this would undoubtedly be a powerful fluorinating agent which, like cobalt trifluoride, would replace hydrogen by fluorine in methanesulphonyl fluoride. The energy liberated during the last reaction would be dissipated efficiently in the liquid reaction medium and through the electrodes, and C–C, C–S, C–O, S–O, etc., fission, so prevalent in vapour-phase fluorination, could thus be substantially prevented.

Examination of the electrolysis cell after the preparation of trifluoromethanesulphonyl fluoride showed that a pale green friable solid had been deposited on the anodes, *i.e.*, on alternate electrodes. The cathodes remained bright and unattacked. The bottom of the cell also contained the pale green solid which had dropped from the anodes. The solid is mainly nickel difluoride, but is not analytically pure, and attempts to purify it failed; its formation on only the anodes supports the proposal of fluorination *via* nickel tri- or tetra-fluoride.

The relatively extensive breakdown caused when trifluoromethanesulphonic acid or moisture is present can be attributed to discharge of hydroxyl ions at the anodes, followed by formation of oxygen difluoride and oxidative attack on methanesulphonic acid or its fluoride present in solution or adsorbed on the anodes.

Trifluoromethanesulphonyl fluoride is hydrolysed by water only very slowly at room temperature, and only slowly by water at 100°. Methanesulphonyl fluoride is hydrolysed

[5] Trott, Brice, Guenther, Severson, Coon, LaZerte, Nirschl, Danielson, Morin, and Pearlson, Amer. Chem. Soc. Meeting, New York, 1954.

much more rapidly (94% compared with 37% by water at 100° in 2 days.) Aqueous sodium or barium hydroxide causes complete hydrolysis within a few minutes to give the corresponding salts. Trifluoromethanesulphonic acid is stable to concentrated nitric acid at 150°.

Barium trifluoromethanesulphonate can easily be obtained pure and is a convenient starting point for the synthesis of other salts, since the barium can easily be removed as sulphate; potassium and silver trifluoromethanesulphonate were thus prepared. The melting points of the potassium, sodium, silver, and barium trifluoromethanesulphonate (230°, 248°, 356°, and >370°) should be compared with those of the corresponding methanesulphonates (>370°, 345°, 263°, and >360°).

Trifluoromethanesulphonyl fluoride is a convenient starting point for synthesis of derivatives of trifluoromethanesulphonic acid, *e.g.*, :

$$CF_3{\cdot}SO_2F \xrightarrow{R_2NH} CF_3{\cdot}SO_2{\cdot}NR_2 \quad (R = H \text{ or } Et)$$

Trifluoromethanesulphonamide, which sublimes *in vacuo*, is readily soluble in water. Its *NN*-diethyl derivative is a liquid which is only slightly soluble in water.

Trifluoromethanesulphonyl fluoride fails to react with ethanol at 100°. Excess of ethanolic sodium ethoxide converts it into sodium trifluoromethanesulphonate; ethyl ether is also formed, thus showing that ethyl trifluoromethanesulphonate reacts further :

$$CF_3{\cdot}SO_2F \xrightarrow{EtONa} CF_3{\cdot}SO_2Et \xrightarrow{EtONa} CF_3{\cdot}SO_3Na + Et_2O$$

The ethyl ester is best prepared by reaction of ethereal silver trifluoromethanesulphonate with ethyl iodide. The methyl ester was prepared by reaction of anhydrous silver trifluoromethanesulphonate with methyl iodide. The esters soon develop an acid reaction to litmus, although prolonged heating with water is necessary to achieve complete hydrolysis.

Infrared Spectra.—The spectra of compounds containing the $-SO_2-$, $-SO_3^-$, or $-SO_2-O-$ groups prepared during the present work are summarised and compared with other spectra in the Table.

The arguments in favour of the assignments of the symmetric (st.-s.) and asymmetric (st.-a.) stretching vibrations of the $-SO_2-$ group in sulphonyl halides have already been given.[2] In particular the 8·07 μ band was preferred for the st.-s. vibration in trifluoromethanesulphonyl chloride rather than that at 8·90 μ, since there is then a shift to shorter wavelength with increase in inductive effect of R in $R{\cdot}SO_2Cl$ along the series R = CH_3, CCl_3, or CF_3, as expected. A similar problem arises in the series $R{\cdot}SO_2F$, since trifluoromethanesulphonyl fluoride shows strong bands at 6·77 μ (st.-a.) and at 8·07 and 8·69 μ. Either of the last two bands could be assigned to the st.-s. vibration or to a C–F stretching vibration, and the fact that the 8·07 μ band is at precisely the same position as one in trifluoromethanesulphonyl chloride favours the assignment of this band in both compounds to the C–F vibration, with the 8·69 and 8·90 μ bands as st.-s. vibrations for $-SO_2F$ and $-SO_2Cl$ respectively, the shift to shorter wavelength being caused by the greater inductive effect of fluorine. A final decision cannot be made with the evidence currently available, but the 8·07 μ band in the trifluoromethanesulphonyl halides is given slight preference for the st.-s. vibration to maintain the sequence SO_2Cl_2 8·30, $CH_3{\cdot}SO_2Cl$ 8·07, $CF_3{\cdot}SO_2F$ 8·07, SO_2F_2 7·88 μ, and to maintain the difference in wavelength (1·0—1·4 μ) between the st.-a. and st.-s. wavelengths observed for all the other compounds which contain the $-SO_2-$ group.

Unsubstituted aliphatic sulphur compounds which contain the $-SO_2-$ group (*e.g.*, sulphonal) show the st.-a. and st.-s. vibrations at *ca.* 7·6 μ and 8·9 μ. Substitution of hydrogen by chlorine in the molecule causes a distinct shift to shorter wavelength. The aromatic sulphonyl fluorides show a further shift to shorter wavelength with absorption at *ca.* 7·10 and 8·25 μ. There is thus a shift to shorter wavelength of these vibrations in the series $R{\cdot}SO_2X$ with X = $C_{aliph.} > C_{arom.} > S > Cl > F$ and with R = Alkyl ~ Aryl > perchloroalkyl > perfluoroalkyl.

The st.-a. and the st.-s. vibrations of the nitro-group in *m*-nitrobenzenesulphonyl fluoride are clearly at 6·50 and 7·40 μ, regions which are free from strong bands in the

Compound [a]		C.S. no.	Asymmetric stretching μ	Symmetric stretching μ	Difference (st.-s.) — (st.-a.) μ
Acid halides and sulphones.					
SO_2F_2 [c]	(v)	—	6·66	7·88	1·22
$CF_3{\cdot}SO_2F$ [b]	(v)	283	6·77	8·07 or 8·69	1·30 or 1·92
$CF_3{\cdot}SO_2Cl$ [c]	(v)	—	6·95	8·07 or 8·90	1·12 or 1·95
SO_2Cl_2 [c]	(v)	—	6·96	8·30	1·34
$CH_3{\cdot}SO_2F$ [c]	(v)	284	6·90, 6·97 [d]	8·20	1·27
	(l)	285	7·20	8·30	1·10
$CCl_3{\cdot}SO_2Cl$ [c]	(v)	—	7·04	8·42	1·38
	(N)	—	7·12	8·45	1·33
$CH_3{\cdot}SO_2Cl$ [a, b]	(v)	286	7·15	8·42	1·27
	(l)	—	7·33	8·53	1·20
$Ph{\cdot}SO_2F$ [b]	(l)	287	7·10	8·27	1·17
$m\text{-}NO_2{\cdot}C_6H_4{\cdot}SO_2F$ [b]	(N)	288	7·07	8·26	1·19
$p\text{-}Cl{\cdot}C_6H_4{\cdot}SO_2F$ [b]	(N)	289	7·10	8·25	1·15
$(Et{\cdot}SO_2)_2CCl_2$ [b]	(N)	—	7·52	8·74	1·22
$(Et{\cdot}SO_2)_2CH_2$ [b]	(N)	—	7·55	8·90	1·35
$[(Et{\cdot}SO_2)_2CH]_2CH_2$ [b]	(N)	—	7·60	8·99	1·39
$(Et{\cdot}SO_2)_2CMe_2$ [b]	(N)	290	7·65	9·02 or 8·62	1·37 or 0·97
$(cyclo\text{-}C_6H_{11})_2SO_2$ [a]	(S)	—	7·62	8·85	1·23
Ph_2SO_2 [a]	(S)	—	7·48	8·59	1·11
Sulphonamides.					
$CF_3{\cdot}SO_2{\cdot}NH_2$ [b]	(N)	291	7·40	8·48	1·08
	(S)	—	7·07	8·72	1·65
$CF_3{\cdot}SO_2{\cdot}NEt_2$ [b]	(l)	292	7·23	8·45 (8·84)	1·22
	(S)	—	7·20	8·45 (8·84)	1·25
$CH_3{\cdot}SO_2{\cdot}NH_2$ [c]	(N)	—	7·49	8·55	1·06
	(S)	—	7·34	8·61	1·27
$Ph{\cdot}SO_2{\cdot}NH_2$ [c]	(N)	—	7·49	8·62	1·13
$CH_3{\cdot}SO_2{\cdot}NHMe$ [c]	(S)	—	7·50	8·62	1·12
Alkyl trifluoromethanesulphonates.					
$CF_3{\cdot}SO_2{\cdot}OMe$ [b]	(l)	293	7·08	8·30 or 8·74	1·22 or 1·66
	(v)	294	6·97	8·15 or 8·65	1·18 or 1·68
$CF_3{\cdot}SO_2{\cdot}OEt$ [b]	(l)	295	7·07	8·30 or 8·74	1·23 or 1·67
	(v)	296	6·97	8·17 or 8·65	1·20 or 1·68
Metal sulphonates.					
$CF_3{\cdot}SO_2Na$ [c]	(N)	137	7·82	9·60	1·78
$CF_3{\cdot}SO_2K$ [b]	(N)	297	7·95	9·70	1·75
$(CF_3{\cdot}SO_2)_2Ba$ [c, d]	(N)	139	7·92	9·62	1·70
$CF_3{\cdot}SO_2Ag$ [c]	(N)	138	7·90	9·75	1·85
$CH_3{\cdot}SO_2Na$ [c, e]	(N)	136	8·37	9·43	1·06
$CH_3{\cdot}SO_2K$ [b]	(N)	298	8·30	9·46	1·16
$(CH_3{\cdot}SO_2)_2Ba$ [b]	(N)	299	8·44	9·41	0·97
$CH_3{\cdot}SO_2Ag$ [b]	(N)	300	8·43	9·45 or 9·73	1·02 or 1·30
$[CH_3{\cdot}(SO_2Na)]_2$ [c]	(N)	—	8·45	9·60	1·15
$CH_2{:}CH{\cdot}SO_2Na$ [b]	(N)	—	8·45	9·55	1·10
$Et{\cdot}SO_2Na$ [f]		—	8·50	9·50	1·00
$Pr{\cdot}SO_2Na$ [f]		—	8·46	9·54	1·08
$Bu{\cdot}SO_2Na$ [f]		—	8·50	9·58	1·08
KSO_2F [b]		—	7·75	9·29	1·54

[a] v = vapour, l = liquid, N = Nujol mull, S = solution in CCl_4.
[b] Parts I and II, refs. 1 and 2. [c] Present work. [d] Baxter, Cymerman-Craig, and Willis, *J.*, 1955, 669. [e] The band at 7·85 μ reported in Parts I and II moves to 7·92 μ when the salt is recrystallised several times. [f] The band at 9·50 μ reported in Parts I and II moves to 9·43 μ when the salt is recrystallised. [g] Raman spectra: Houlton and Tartar, *J. Amer. Chem. Soc.*, 1938, **60**, 544.

spectrum of benzenesulphonyl fluoride. The C–H vibration in the arylsulphonyl fluorides appears at 6·88, 6·80, and 6·78 μ respectively for the two compounds shown in the Table.

The spectrum of solid trifluoromethanesulphonamide resembles that of methanesulphonamide. The $-SO_2-$ vibrations are well defined and lie at shorter wavelength for the fluoro-compound. The C–F stretching vibrations are at 8·11 and 8·69 μ. The N–H stretching vibrations are at 2·96 and 3·05 μ for solid trifluoromethanesulphonamide (cf. 2·69, 3·06, and 3·20 μ for $CH_3{\cdot}SO_2{\cdot}NH_2$ and 2·98 and 3·06 μ for $Ph{\cdot}SO_2{\cdot}NH_2$) and at 2·89, 2·99 μ for its solution in carbon tetrachloride (cf. 2·90 and 2·98 μ and 2·90 and 2·98 μ for

similar solutions of $CH_3{\cdot}SO_2{\cdot}NH_2$ and $Ph{\cdot}SO_2{\cdot}NH_2$). The $-SO_2-$ vibrations for *NN*-diethyltrifluoromethanesulphonamide are scarcely changed at 7·20 and 8·45 or 8·84 μ for a solution in carbon tetrachloride compared with a spectrum of the liquid (see Table). Trifluoromethanesulphonamide is markedly associated in the solid, however, since the strong bands assigned to the $-SO_2-$ vibrations for the solid (7·40, 8·48 μ) shift to 7·07, 8·72 μ when the compound is dissolved in carbon tetrachloride. The last pair of bands must be assigned to the st.-a. and the st.-s. vibration of the unassociated amide. The st.-s. vibration for *NN*-diethyltrifluoromethanesulphonamide is thus probably at 8·84 rather than at 8·48 μ.

The st.-a. band in the alkyl trifluoromethanesulphonates is quite clear at *ca.* 7 μ, but more than one band could plausibly be assigned to the st.-s. vibration (see Table). Slight preference can be given to the band at lower wavelength in view of the assignments for trifluoromethanesulphonyl fluoride, but unambiguous distinction cannot yet be made. The liquid methyl ester shows a characteristic strong band at 12·45 and the ethyl ester one at 10·77 μ.

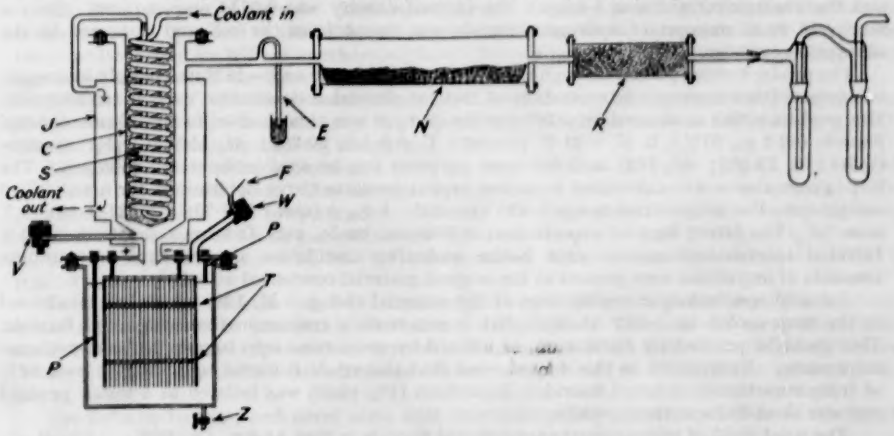
Further examples of metal sulphonates and trifluoromethanesulphonates enable a better comparison of infrared spectra to be made than was possible earlier.[1,2] Metal alkanesulphonates absorb strongly at 8·4—8·6 μ (st.-a.) and 9·4—9·6 μ (st.-s.). Introduction of fluorine causes shift of the st.-a. vibration to shorter wavelength (7·8—7·95 μ) with hardly any change in the st.-s. vibration. The C–F stretching vibration in sodium, potassium, or silver trifluoromethanesulphonates lies near 8·5 μ.

The st.-a. and the st.-s. vibration of the $-SO_2-$ group in the $F{\cdot}SO_2{\cdot}O^-$ ion lie at 7·75 and 9·29 μ, and this fits well into the metal sulphonate series, since replacement of CF_3 in $CF_3{\cdot}SO_2{\cdot}O^-$ by the more electronegative fluorine would be expected to cause a shift to shorter wavelength.

Experimental

Apparatus.—The electrolytic cell is shown diagrammatically in the Figure, and is modelled on that described earlier,[4] with improvements resulting from prolonged operation of such cells. The

Laboratory cell for electrochemical fluorination in anhydrous hydrogen fluoride.



cell body was a flanged nickel cylinder, 15 cm. long and 8 cm. in diameter, with silver-soldered joints, and with a small nickel valve (*Z*) for drainage. The 22 electrodes (each 12·7 × 6·3 × 0·17 cm.) served as alternate anodes and cathodes with a total surface area of *ca.* 3500 sq. cm. They were insulated from each other by Teflon spacers (*T*), and their leads, by which they were suspended from the nickel lid, were also insulated by Teflon bushings. A 3 mm. Teflon gasket clamped by 12 bolts rendered the flange leakproof. The two electrical probes (*P*) extended to two-thirds of the depth of the cell and to near the top of the electrode assembly respectively, and provided an easy method for determination of electrolyte level. In the centre of the lid was an exit tube leading to the efficient condenser (*C*), the cold finger of which was 16 cm. long,

4 cm. in diameter, and 5 mm. from the outer tube of the condenser. The efficiency of the condenser was greatly improved by a jacket (*J*) which cooled the outside of the outer tube of the condenser. Gas issuing from the cell had thus to pass up a 5 mm. annular tube cooled on both sides. The jacket (*J*) was welded to the outer tube of the condenser, and the aqueous glycol coolant was circulated rapidly at −5° by means of a powerful pump through the cooling spiral(*S*), then passed through *J*. The cold finger was filled with ethanol to provide contact between the cooling spiral and the inner wall of the condenser. The cell was filled with hydrogen fluoride (580 ml.) to the upper probe by means of the nickel valve *V*. The hydrogen fluoride was sufficiently anhydrous to render preliminary electrolysis unnecessary. Solute was added to the cell through a nickel valve (*W*) by means of the small nickel funnel (*F*).

A nickel tube led from the top of the condenser *via* a safety tube dipped in mercury (*E*) to a flanged copper cylindrical tube (*N*) (67 × 7 cm.) which contained a tray of sodium fluoride pellets (300 g.) to remove hydrogen fluoride swept through the condenser; the tube was heated to 60° to prevent possible condensation or adsorption of products. The cell gases then passed through a flanged cylindrical copper tube (*R*) (23 × 4 cm.) which contained 1 cm. squares of rubber sheet (100 g.) to absorb oxygen fluoride. The condensable products then collected in traps cooled at −78° and −183°, and the hydrogen and entrained carbon tetrafluoride were allowed to escape to atmosphere.

Methanesulphonyl Chloride.—A commercial sample was redistilled from phosphoric oxide (Found : S, 27·9. Calc. for CH_3O_2ClS : S, 27·7%).

Methanesulphonyl Fluoride.—Methanesulphonyl chloride (200 g.) was added with stirring to a suspension of potassium hydrogen difluoride (150 g.) in water (115 ml.) at 20°. After being stirred for 30 min. the mixture was steam-distilled, and the lower layer so obtained was separated, dried (Na_2SO_4), and distilled to give methanesulphonyl fluoride (144 g., 84%), b. p. 123—124° (Found : C, 12·7; H, 3·0. Calc. for CH_3O_2FS : C, 12·2; H, 3·1%). Davies and Dick [a] report b. p. 124·2° for a specimen prepared by prolonged reaction of methanesulphonyl chloride and zinc fluoride. The method used is based on that briefly reported in B.P. 628,796/1949.

Electrochemical Fluorination of Methanesulphonyl Fluoride.—In a typical experiment methanesulphonyl fluoride (30·0 g.) was added to anhydrous hydrogen fluoride (580 g.) in the cell to give a 5·2% solution by wt. Electrolysis was begun at 5 v and 6·4 amp., and during approx. 15 hr. the current fell steadily to 2·8 amp.; a voltage of 5 v was maintained during the electrolysis, and the average current was 5 amp. The current density was 0·0014 amp./sq. cm. Only a relatively small amount of hydrogen fluoride was swept from the cell and appeared in the absorption cylinder.

The product which passed through the traps cooled at −78° and −183° was mainly hydrogen, but infrared spectroscopic examination of the gas showed it to contain carbon tetrafluoride. The product which condensed at −78° was distilled; it was almost all *trifluoromethanesulphonyl fluoride* (42·5 g., 91%), b. p. −21·7° (Found : C, 8·0; S, 20·7%; *M*, 152. CO_3F_4S requires C, 7·9; S, 21·0%; *M*, 152), and for most purposes can be used without redistillation. The b. p. given above was calculated from the vapour-pressure curve determined for a redistilled sample over the temperature range −47° to −24° : $\log_{10} p$ (mm.) = 7·736 − 1221/*T* where *T* is in °K. The latent heat of vaporisation is 5590 cal./mole, and Trouton's constant is 22·2. Infrared spectroscopic examination before and after distillation showed that only minute amounts of impurities were present in the original material condensed at −78°.

Infrared spectroscopic examination of the material (3·2 g.; *M*, 128) which had condensed in the trap cooled at −183° showed that it was mainly trifluoromethanesulphonyl fluoride. This could be purified by distillation, or utilised by conversion into barium trifluoromethanesulphonate. Purification in this way showed that this crude material contained at least 66% of trifluoromethanesulphonyl fluoride; fluoroform (1% yield) was isolated as a minor product and was identified spectroscopically.

The total yield of trifluoromethanesulphonyl fluoride is thus 44·6 g., *i.e.*, 96%.

Electrochemical Fluorination of Methanesulphonyl Chloride.—The chloro-compound (25·0 g.), dissolved in 580 g. of anhydrous hydrogen fluoride (*i.e.*, 4·3% solution by wt.), was electrolysed under the conditions described above, for 19 hr. The initial current of 4·2 amp. fell to 2·2 amp. during this time, with the voltage maintained at 5 v.

The product which condensed in a trap cooled to −78° was distilled to give trifluoromethanesulphonyl fluoride (28·8 g., 87%), b. p. −21·7° (Found : *M*, 152). Infrared spectroscopy showed that it was identical with the compound described above, and in particular was free

[a] Davies and Dick, *J.*, 1932, 483.

from trifluoromethanesulphonyl chloride. The small amount of impurity detected spectroscopically was the same as that obtained from methanesulphonyl fluoride.

Hydrolysis of Trifluoromethanesulphonyl Fluoride.—(a) *With water.* Trifluoromethanesulphonyl fluoride (0·994 g.) and water (5 ml.) were shaken vigorously in a sealed tube at 20° (48 hr.). Only 7% of the fluoride had then been hydrolysed, and spectroscopic examination of the volatile products revealed only starting material.

In a second experiment trifluoromethanesulphonyl fluoride (0·986 g.) and water (5 ml.), heated at 100° (48 hr.), gave unchanged starting material (63%) as gaseous product. The aqueous solution was neutralised with sodium carbonate and evaporated to dryness. The residue was extracted with dry acetone, and evaporation of the acetone solution, followed by crystallisation from acetone, gave sodium trifluoromethanesulphonate (0·370 g., 90% based on $CF_3{\cdot}SO_2F$ hydrolysed). The infrared spectrum of the salt was identical with that described in Part I.[1]

(b) *With sodium hydroxide.* Trifluoromethanesulphonyl fluoride (1·064 g.), sodium hydroxide (1 g.), and water (10 ml.) were shaken vigorously in a sealed tube at 20° (4 hr.). Quantitative hydrolysis occurred to give sodium trifluoromethanesulphonate (1·11 g., 92%), isolated by acetone extraction of the dried aqueous solution followed by recrystallisation from acetone.

(c) *With barium hydroxide.* Complete hydrolysis occurred when trifluoromethanesulphonyl fluoride (1·070 g.) was shaken with barium hydroxide octahydrate (4 g.) and water (50 ml.) at 20° (1 hr.). The aqueous solution was slightly acidified with dilute sulphuric acid to precipitate the excess of barium as sulphate, and the slight excess of sulphuric acid was removed by addition of an excess of solid barium carbonate. The solution was filtered, evaporated to dryness, then extracted with acetone to give barium trifluoromethanesulphonate (100%).

A portion (0·913 g.) of the product obtained in the trap at −183° during the electrochemical fluorination of methanesulphonyl fluoride, shaken with aqueous barium hydroxide (48 hr.), gave fluoroform (0·014 g., 1%) as the main residual volatile product, and barium trifluoromethanesulphonate (0·87 g., 66%), isolated as above, in the aqueous solution.

Hydrolysis of Methanesulphonyl Fluoride.—(a) *With water.* Methanesulphonyl fluoride (0·946 g.) and water (5 ml.), heated at 100° (48 hr.) under conditions similar to those used with trifluoromethanesulphonyl fluoride (above), gave unchanged methanesulphonyl fluoride (0·054 g., 6%) and methanesulphonic acid (94%).

(b) *With barium hydroxide.* Methanesulphonyl fluoride (1·080 g.), barium hydroxide octahydrate (4 g.), and water (50 ml.) were shaken at room temperature (1 hr.) under the conditions used for trifluoromethanesulphonyl fluoride (above). The fluoride was completely converted into barium methanesulphonate.

Derivatives of Trifluoromethanesulphonic Acid.—(a) *Salts.* The sodium salt, prepared as above, recrystallised from acetone and dried to constant weight *in vacuo* at 140°, had m. p. 248°. The barium salt, similarly treated, had m. p. >370°.

Barium trifluoromethanesulphonate (0·77 g.) was dissolved in water (5 ml.), and treated with dilute sulphuric acid. The filtered barium-free solution was then neutralised with potassium carbonate and evaporated to dryness, and the residual solid was extracted with acetone, evaporation of which gave *potassium trifluoromethanesulphonate* (0·56 g., 84%) (Found : K, 20·7. CO_3F_3SK requires K, 20·8%); recrystallised from acetone and dried at 140°/10^{-3} mm., it had m. p. 230°.

To a solution of barium trifluoromethanesulphonate (0·62 g.) in water (5 ml.) was added dilute sulphuric acid to precipitate the barium. The filtered solution was neutralised with silver carbonate, then evaporated to dryness; the residual silver trifluoromethanesulphonate (0·69 g., 95%), recrystallised from benzene–carbon tetrachloride or ether–carbon tetrachloride, had m. p. 356°.

The sodium, barium, and silver salts were spectroscopically identical with those described in Part I.[1]

(b) NN-*Diethyltrifluoromethanesulphonamide.* Trifluoromethanesulphonyl fluoride (3·0 g.) and anhydrous diethylamine (4·2 g.) reacted immediately, a solid being deposited; after being kept overnight in a sealed tube the products were treated with water (25 ml.) which caused separation of a lower layer. This and the ethereal extract of the aqueous layer were dried (Na_2SO_4) then distilled, to give NN-*diethyltrifluoromethanesulphonamide* (3·3 g., 83%), b. p. 55°/7 mm. (Found : C, 29·4; H, 5·2; N, 7·1. $C_5H_{10}O_2NF_3S$ requires C, 29·3; H, 4·9; N, 6·8%). The amide is soluble in the common organic solvents but not in water.

(c) *Trifluoromethanesulphonamide.* Anhydrous ammonia (0·88 g.) and trifluoromethanesulphonyl fluoride (3·10 g.) reacted immediately in a sealed tube, with deposition of solid.

Extraction with chloroform and evaporation of the extracts gave *trifluoromethanesulphonamide* (2·37 g., 78%), m. p. (after sublimation *in vacuo*) 119° (Found: C, 8·1; H, 1·3; N, 9·7. $CH_2O_2NF_3S$ requires C, 8·1; H, 1·3; N, 9·4%). The amide dissolves in water.

(d) *Ethyl trifluoromethanesulphonate.* Trifluoromethanesulphonyl fluoride (5·0 g.) and anhydrous ethanol (5 ml.) formed two layers and failed to react in a sealed tube at 100° during 24 hr.

Trifluoromethanesulphonyl fluoride (9·84 g.), sodium (3·0 g.), and anhydrous ethanol (50 ml.) reacted exothermically in a sealed tube at room temperature (1 hr.). Ethyl ether and excess of ethanol were the only volatile products obtained when the solution was evaporated. Extraction of the residual solid with acetone, followed by evaporation of the acetone, gave sodium trifluoromethanesulphonate (9·30 g., 84%).

Silver trifluoromethanesulphonate (10·0 g.) was suspended in anhydrous ether (50 ml.) and stirred whilst ethyl iodide (8·0 g.) was added. Immediate precipitation of silver iodide occurred and the reaction was completed by heating under reflux (30 min.). The ethereal solution was decanted from the silver iodide (100%), and distillation of the ethereal solution gave *ethyl trifluoromethanesulphonate* (5·1 g., 74%), b. p. 115° (Found: C, 19·9; H, 2·7. $C_3H_5O_3F_3S$ requires C, 20·2; H, 2·8%). The ester reacted only slowly with water or aqueous alkali but rapidly turned blue litmus red.

(e) *Methyl trifluoromethanesulphonate.* Silver trifluoromethanesulphonate (12·1 g.) was shaken whilst methyl iodide (6·3 g.) was added. When the vigorous reaction subsided, the volatile products were distilled *in vacuo* from the silver iodide produced, then redistilled to give *methyl trifluoromethanesulphonate* (4·4 g., 69%), b. p. 99° (Found: C, 14·8; H, 2·1. $C_2H_3O_3F_3S$ requires C, 14·6; H, 1·8%).

Stability of Trifluoromethanesulphonic Acid to Nitric Acid.—Sodium trifluoromethanesulphonate (0·84 g.), heated with concentrated nitric acid (5 ml.) in a sealed tube at 150° (48 hr.), liberated not even a trace of fluoride ion. Neutralisation with sodium carbonate followed by acetone extraction of the solid from the evaporated solution gave sodium trifluoromethanesulphonate (82%).

Salts of Methanesulphonic Acid.—Sodium, potassium, barium, and silver methanesulphonates were prepared from the acid by neutralisation with the corresponding carbonate. They were recrystallised from aqueous ethanol or aqueous acetone and dried to constant weight *in vacuo* at 140° (90° for the silver salt). Spectroscopic examination then showed them to be free from water. The following m. p.s were determined: $CH_3{\cdot}SO_3Na$ 345°, $CH_3{\cdot}SO_3K$ >360°, $(CH_3{\cdot}SO_3)_2Ba$ >360°, $CH_3{\cdot}SO_3Ag$ 263°.

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University Chemical Laboratory, Cambridge. [*Received, August 8th*, 1955.]

34. *Mannose-containing Polysaccharides. Part IV.* The Glucomannans of Lily Bulbs.*

By P. Andrews, L. Hough, and J. K. N. Jones.

Glucomannans isolated from bulbs of *Lilium candidum*, *L. henryii*, and *L. umbellatum* showed similar physical properties and were each constituted of D-glucose and D-mannose (*ca.* 1 : 2 parts) but apparently in slightly different proportions.

Structural studies of *L. umbellatum* and *L. henryii* glucomannan polysaccharides suggested that the majority of the hexose units were linked together by 1 : 4-β-glycosidic bonds to form long chains which were terminated at their non-reducing ends by D-glucopyranosyl units. These two polysaccharides differed in their average chain lengths. *L. umbellatum* glucomannan had a small number of glucopyranosyl units as branching points linked through $C_{(1)}$, $C_{(3)}$, and $C_{(6)}$.

Few glucomannans have been examined in detail although several have been isolated from plants as, for example, by extraction of the tubers of *Amorphophallus konjak* [1] and *A. oncophyllus*,[2] the leaves of *Aloe vera*,[3] the roots of *Cremastra variabilis* and *Bletilla striata*,[4] and the bulbs of *Narcissus tazetta*.[5] None of these glucomannans appeared to contain more glucose than mannose but, since physical homogeneity was not established, they could have been mixtures. "Iles Mannan," extracted from tubers of *Amorphophallus* plants, has been separated into an amylose-type polysaccharide (1 part) and a glucomannan (6 parts), the latter containing mainly D-glucopyranosyl and D-mannopyranosyl units (in approximately 1 : 2 ratio) joined by 1 : 4-β-glycosidic linkages.[6]

Lily bulbs contain in addition to starch a reserve polysaccharide, which exists as a water-soluble mucilage in the parenchymatous cells of the bulb scales.[7] Takahashi [8] found twice as much mannose as glucose in the polysaccharide which formed an insoluble copper complex.

Extraction of the bulbs of *L. umbellatum*, *L. henryii*, and *L. candidum* with cold water gave in each case a glucomannan (the yield varying with the species), but none of these three products contained starch components. After purification *via* their copper complexes, these polysaccharides became insoluble in water, perhaps because of a change in the conformation of the hexopyranoside rings during complex formation, as has been observed in the case of amylose in alkaline solution.[9] The three glucomannans showed similar optical rotations ($[\alpha]_D$ *ca.* −26°, −21°, −25° respectively) and resemble the glucomannan ($[\alpha]_D$ −21°) from *Amorphophallus*,[6] in that they all contained D-glucose and D-mannose in the approximate ratio of 1 : 2 respectively; however, in the case of the three *Lilium* glucomannans, the proportions differed slightly (1 : 1·83; 1 : 1·93; 1 : 2·00 respectively). When the *Lilium* glucomannans were heated in 0·01N-sulphuric acid for 7 hr. at 100°, the solutions showed but little increase in reducing power and did not liberate any monosaccharide; thus it was assumed that little, if any, furanose forms of the sugars were present.

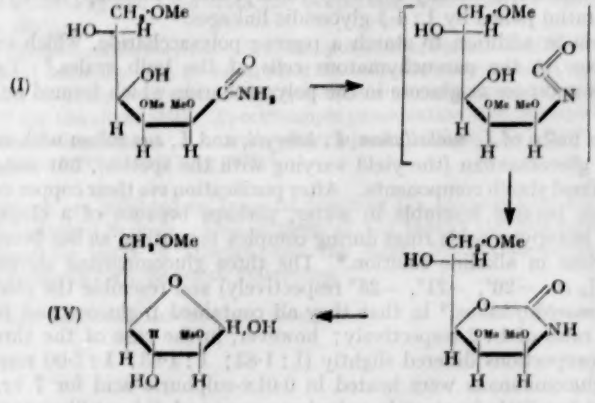
The glucomannans from *L. umbellatum* and *L. henryii* were methylated exhaustively to give methylated products ($[\alpha]_D$ −20°, −23°, in $CHCl_3$, respectively), which on hydrolysis

* Part III, *J.*, 1953, 1186. Some aspects of this work were presented at the 12th International Congress of Pure and Applied Chemistry, New York, 1951.

[1] Otsuki, *Acta Phytochim., Japan*, 1928, **4**, 1; Nishida and Hoshima, *J. Dept. Agric. Kyushu Imp. Univ.*, 1930, **2**, 277.
[2] Wise, *Arch. Biochem.*, 1949, **23**, 127.
[3] Roboz and Haagen-Smit, *J. Amer. Chem. Soc.*, 1948, **70**, 3248.
[4] Otsuki, *Acta Phytochim., Japan*, 1937, **10**, 1, 29.
[5] Kihara, *J. Agric. Chem. Soc. Japan*, 1931, **7**, 1061.
[6] Rebers and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 6097.
[7] Parkin, *Proc. Cambridge Phil. Soc.*, 1901, **11**, 139.
[8] Takahashi, *J. Agric. Chem. Soc. Japan*, 1930, **6**, 791, 861; 1931, **7**, 219.
[9] Reeves, *J. Amer. Chem. Soc.*, 1954, **76**, 4595.

yielded similar mixtures of *O*-methyl sugars, consisting mainly of tri-*O*-methylhexoses with small amounts of tetra- and di-*O*-methylhexoses, which were separated by chromatography on cellulose. In the tetra-*O*-methyl fractions, only 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose could be detected and a quantitative estimate suggested that it formed 3·7% and 1·3% of the respective *O*-methyl sugar mixtures. Although the tri-*O*-methylhexose fractions showed on paper chromatograms only one spot, which corresponded with that given by both 2 : 3 : 6-tri-*O*-methyl-D-mannose ($[\alpha]_D$ −7°) and 2 : 3 : 6-tri-*O*-methyl-D-glucose ($[\alpha]_D$ +70·5°), the optical rotation (+ 19°) of each fraction was suggestive of mixtures of these two monosaccharides in the approximate ratio of 2 : 1 respectively. The difficulty in separating, and thus identifying, these two *O*-methyl sugars was circumvented in each case by oxidation to their corresponding mixed lactones, which were separated by chromatography on cellulose and then converted into characteristic crystalline derivatives. Rebers and Smith,[9] who worked with a similar mixture, overcame this difficulty by treating the mixture with cold methanolic hydrogen chloride, when only the tri-*O*-methylglucose derivative reacted, thus giving a mixture of methyl 2 : 3 : 6-tri-*O*-methyl-D-glucofuranoside and 2 : 3 : 6-tri-*O*-methyl-D-mannose which were separable by chromatography on cellulose.

2 : 3 : 6-Tri-*O*-methyl-D-mannose was characterised as crystalline 2 : 3 : 6-tri-*O*-methyl-D-mannonamide (I). When this amide (I) was degraded with hypochlorite by the Weerman procedure, a crystalline cyclic urethane derivative (III) was produced, presumably *via* the acyclic *iso*cyanate (II) (cf. Ault, Haworth, and Hirst [10]). Degradation of the cyclic urethane derivative (III) with aqueous base gave 2 : 5-di-*O*-methyl-D-arabinose (IV). Haworth, Peat, and Whetstone [11] carried out a similar degradation using 2 : 3 : 6-tri-*O*-methyl-D-gluconamide.



Demethylation of the di-*O*-methyl fraction from the methylated *L. henryii* glucomannan revealed the presence of both glucose and mannose derivatives. At least three di-*O*-methyl derivatives were detected on paper chromatograms, but these were not identified because of the small quantities available, and hence their significance cannot be assessed. They could have arisen from incomplete methylation of the polysaccharide, from demethylation during hydrolysis, and from branching points in the polysaccharide. In contrast, the *L. umbellatum* methylated glucomannan yielded a di-*O*-methylhexose fraction which contained mainly 2 : 4-di-*O*-methyl-D-glucose. On paper chromatograms, it gave only one spot which was indistinguishable from that from an authentic specimen, and on demethylation only glucose was detected; its derived lactone showed a rapid change in optical rotation in aqueous solution (indicating a 4-methoxyl group), and the derived amide gave only a very slight Weerman test for an α-hydroxy-amide (indicating a

[10] Ault, Haworth, and Hirst, *J.*, 1934, 1722.
[11] Haworth, Peat, and Whetstone, *J.*, 1938, 1975.

2-methoxyl group). 2 : 4-Di-*O*-methyl-D-glucose could not have arisen by either under-methylation or demethylation from a 1 : 4-linked polymer (cf. Andrews, Hough, and Jones [12]) and must therefore represent a branching point.

Thus methylation studies of *L. umbellatum* glucomannan indicated that it contained chains of D-glucopyranosyl and D-mannopyranosyl units linked through $C_{(1)}$ and $C_{(4)}$ with an average of about 27 hexose units per non-reducing end group. Only D-glucopyranosyl units were detected as non-reducing end groups, and the chains were joined by a small number of D-glucopyranosyl units linked through $C_{(1)}$, $C_{(3)}$, and $C_{(6)}$ (branching points). The molecular ratio of tetra-*O*-methylglucose to di-*O*-methylglucose was found to be 1·0 to 0·65, suggesting an average of about two branching points per molecule. Methylation evidence suggested that *L. henryii* glucomannan contained mainly 1→4 linked hexopyranosyl units, but with an average chain length of about 75 hexose units per D-glucopyranosyl end group. Attempts to obtain structural information by periodate oxidation of the polysaccharides were unsuccessful, since only a steady liberation of formic acid was observed. The optical rotations of the glucomannans and of their methylated derivatives suggested that the majority of the inter-glycosidic linkages were of the β-type.

The *Lilium* glucomannans thus show a marked structural resemblance to the *Amorphophallus* glucomannan,[6] although in this case neither end groups nor branching points were detected. It is of interest to compare the *Lilium* glucomannans with the polysaccharides of Iris seeds,[13] since both are constituted of chains of D-glucopyranosyl and D-mannopyranosyl units linked through $C_{(1)}$ and $C_{(4)}$. However, in *L. umbellatum* and *L. henryii* glucomannans, the non-reducing end groups were mainly, if not all, D-glucopyranosyl, whereas only D-galactopyranosyl was detected as non-reducing end group in the *Iris* polysaccharides. In mannans A and B from ivory nut the majority of the D-mannopyranosyl residues are linked through $C_{(1)}$ and $C_{(4)}$, and both D-mannopyranosyl and D-galactopyranosyl units were found as end groups.[14]

Experimental

Paper chromatography was by the descending method,[15] on Whatman No. 1 filter paper and with the following solvent systems: (*a*) ethyl acetate–acetic acid–water (9 : 2 : 2 v/v); (*b*) butan-1-ol–pyridine–water (10 : 3 : 3 v/v); (*c*) butan-1-ol–ethanol–water (40 : 11 : 19 v/v); (*d*) benzene–ethanol–water (34 : 10 : 3 v/v; top layer, clarified with a little ethanol) (for methylated sugars only). Sugars were detected on the chromatograms with ammonical silver nitrate,[16] aniline phthalate or *p*-anisidine hydrochloride.[16] The rate of movement of methyl sugars is quoted relative to that of tetra-*O*-methylglucopyranose (R_G = 1·00).

Unless otherwise stated, solutions were concentrated under reduced pressure and optical rotations were determined in water at 20° ± 2°.

Preliminary Treatment of the Bulbs.—The bulbs of each species were shredded, washed with methanol, and then macerated with this solvent. After 7 days, the insoluble material was collected on a cheese-cloth, and the extraction process repeated. The insoluble material was then dried under reduced pressure first at room temperature and then at 50°. The crisp solids so obtained were milled and gave cream-coloured powders. The methanolic filtrates when evaporated yielded thick, brown syrups in which the presence of sucrose, glucose, fructose, and amino-acids was indicated by paper chromatography. Treatment of the macerated bulbs with methanol for two weeks appeared to inactivate the polysaccharidases as no degradation of the glucomannans was noted during aqueous extraction.[17]

Preparation of the Glucomannans.—The glucomannans were isolated by extraction of the bulb powder with cold water (3 l. per 100 g. of powder) for 18 hr. Starch, the other main polysaccharide component, was not extracted by this process, as indicated by the absence of blue colour when iodine solution was added to the aqueous extract. The starch could be isolated by extraction with hot water or dilute alkali. After clarification of the cold-water extracts on the

[12] Andrews, Hough, and Jones, *J.*, 1954, 806.
[13] *Idem*, *J.*, 1953, 1186.
[14] Aspinall, Hirst, Percival, and Williamson, *J.*, 1953, 3184.
[15] Partridge, *Biochem. J.*, 1948, **42**, 238.
[16] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[17] Husemann, *J. prakt. Chem.*, 1940, **155**, 241.

centrifuge, the supernatant liquors were poured into ethanol to precipitate the glucomannans. After several re-precipitations by slow addition of ethanol to their aqueous solutions, the glucomannans were isolated on the centrifuge, washed with ethanol, and ether, and dried over phosphoric oxide at 20° under reduced pressure. The resultant pale, buff-coloured powders dissolved slowly in water to give opaque solutions, probably owing to the presence of a little protein. They gave no colour with iodine solution and had the following properties:

Glucomannan from	Yield (%) from dried bulb	$[\alpha]_D$	N (%)	Sulphated ash (%)
L. umbellatum	5	$-26° \pm 5°$ (*c*, 0·4)	1·5	2·9
L. henryii	20	$-21° \pm 8°$ (*c*, 0·5)	1·0	2·2
L. candidum	14	$-25° \pm 5°$ (*c*, 0·7)	1·0	0·6

The glucomannans were precipitated as blue copper complexes from aqueous solution by Fehling's solution (equal parts of A and B). The copper complexes were soluble in ice-cold 0·1N-hydrochloric acid, from which solutions the glucomannans were precipitated with ethanol. However, even before drying, the glucomannans so treated had become insoluble in water, but remained soluble in sodium hydroxide solution and in formic acid. The mother-liquors from which the insoluble copper complexes had been removed were neutralised with dilute mineral acid, and after dialysis the solutions were evaporated. Hydrolysis of the residues with N-sulphuric acid at 100° for 16 hr., followed by chromatography of the neutralised (barium carbonate) hydrolysates, indicated the presence in each of amino-acids and very small amounts of arabinose; mannose and glucose were absent.

Hydrolysis of the Glucomannans.—The water-soluble glucomannans were hydrolysed in N-sulphuric acid at 100° for 15 hr., and the hydrolysates were neutralised (barium carbonate), filtered, and concentrated. Paper chromatography of each hydrolysate revealed the presence of glucose and mannose, in the approximate ratio of 1 : 2, with traces of arabinose and xylose; uronic acids were not detected.

The two hexoses present in each glucomannan were isolated by hydrolysing each polysaccharide (1—2 g.) as above, and separating the sugars on a column of cellulose (30 × 1·5 cm.) using butan-1-ol, half-saturated with water, as the mobile phase. In each case crystalline D-glucose and D-mannose were isolated and characterised as tabulated, after recrystallisation from methanol.

	D-Glucose			D-Mannose		
Glucomannan from	m. p.	mixed m. p.	$[\alpha]_D$ (equil.)	m. p.	mixed m.p.	$[\alpha]_D$ (equil.)
L. umbellatum	144°	145°	+52·5°	132°	132°	+14°
L. henryii	145	145	+52	132	131	+15
L. candidum	146	145	+52	132	132	+14

For quantitative analyses, the glucomannans (*ca.* 50 mg.) were hydrolysed in sealed tubes with N-sulphuric acid (2 c.c.) as above. To each hydrolysate was added D-ribose (*ca.* 20 mg.) and, after removal of anions with the minimum amount of Amberlite resin IR-4B (carbonate form), the solutions were evaporated. Portions of each of the residual sugar syrups were separated on large sheet-paper chromatograms with solvent (*c*). After recovery from the appropriate paper strips by Soxhlet-extraction with water (5 c.c.), the sugars were estimated in duplicate by the periodate oxidation method of Hirst and Jones.[18] It being assumed that there was complete recovery of the ribose, and that none of the sugars was lost preferentially, the annexed results were obtained.

Glucomannan from	Wt. hydrolysed (mg.)	Hexose found (mg.) (calc. as $C_6H_{12}O_6$) Glucose	Mannose	Recovery * (%)	Mean sugar ratios Glucose : Mannose
L. umbellatum	57·2	17·8, 17·1	32·2, 31·5	87, 85	1·00 : 1·83
L. henryii	49·1	14·2, 14·5	27·0, 28·2	84, 87	1·00 : 1·93
L. candidum	47·2	14·8, 14·6	29·2, 29·3	93, 93	1·00 : 2·00

* Not corrected for ash and protein content.

An estimate of the glucose : mannose ratio in the *L. umbellatum* glucomannan by Jones and Pridham's benzidine colorimetric method [19] gave a value of 1·00 : 1·88.

[18] Hirst and Jones, *J.*, 1949, 1659.
[19] Jones and Pridham, *Biochem. J.*, 1954, **58**, 288.

Periodate Oxidations.—As in the method described by Brown, Halsall, Hirst and Jones,[20] *L. henryii* glucomannan (1·654 g.) was dissolved in water (150 c.c.), and potassium chloride (10 g.) and 0·23M-sodium metaperiodate solution (80 c.c.) were added. The mixture was kept in the dark and frequently shaken. At intervals, portions (10 c.c.) of the clear solution were withdrawn, ethylene glycol (3 c.c.) was added, and the formic acid titrated with 0·009N-sodium hydroxide, methyl-red screened with methylene-blue being used as indicator.

Period of oxidation (hr.)	168	216	240	288	314	360	407	461
Titre (c.c.)	0·77	1·34	1·50	1·52	1·76	1·91	2·22	2·43
Average no. of hexose units yielding 1 mole of formic acid	63	36	33	32	28	26	22	20

The uptake of periodate by the *L. henryii* glucomannan was determined as follows: in each of several bottles was placed glucomannan (43·7 mg.) in water (25 c.c.), together with potassium chloride (0·3 g.) and 0·452N-sodium metaperiodate (3·00 c.c.). After various periods, the mixture in one bottle was made just alkaline with dilute sodium hydroxide, saturated sodium hydrogen carbonate (10 c.c.), excess of potassium iodide, and 0·097N-sodium arsenite (15 c.c.) were added, and the excess of arsenite was titrated with 0·167N-iodine [titres (c.c.): 2·86 (144 hr.), 2·91 (186 hr.), 3·15 (307 hr.), 3·29 (432 hr.)]. These titres correspond to periodate uptakes (mol. per $C_6H_{10}O_5$ unit) of: 0·89, 0·90, 0·98, and 1·02 respectively.

L. candidum glucomannan (1·2064 g.) was suspended in 0·15M-sodium metaperiodate (100 c.c.) at 18° shaken in a brown bottle. At intervals, portions (10 c.c.) were withdrawn, ethylene glycol (2 c.c.) was added, and after 10 min. the solution titrated with 0·01N-sodium hydroxide to pH 6·25 (cf. Anderson, Greenwood, and Hirst [21]) with the following results:

Period of oxidation (hr.)	15	19	21	41	46	65	89	137
Titre (c.c.)	2·1	2·1	2·15	3·7	4·3	5·65	7·2	9·8

In a similar experiment, *L. umbellatum* (1·0787 g.) gave the following results:

Period of oxidation (hr.)	15	19	22	41	46	65	89	137
Titre (c.c.)	3·0	3·2	3·35	4·35	5·3	6·4	7·4	9·1

Methylation.—The *L. umbellatum* and the *L. henryii* glucomannan were treated with methyl sulphate and sodium hydroxide in the usual way.[13] The *L. umbellatum* glucomannan (6 g.) after six methylations gave a product (5 g.) [Found: OMe, 44·6. Calc. for $C_6H_7O_2(OMe)_3$: OMe, 45·6%] which was extracted from the dialysed mixture with chloroform. It was fractionated under reflux for 1 hr. with mixtures (100 c.c.) of chloroform and light petroleum (b. p. 40—60°). In the first extraction pure light petroleum was used. Thereafter the solid was extracted with light petroleum containing 10%, then 20%, and then 30% of chloroform. Each extraction was carried out twice. The main fraction of methylated polysaccharide was a crisp yellow solid (4·2 g.) and was soluble in the mixture containing 80% of light petroleum, but insoluble in the mixture containing 90% of light petroleum.

After 9 methylations, the *L. henryii* glucomannan (3 g.) similarly gave a chloroform-soluble product (1·6 g.) (Found: OMe, 41·9%), which when fractionated with chloroform–light petroleum gave, as the main fraction, a crisp buff solid (1·28 g.) with the same solubility properties as the main *L. umbellatum* fraction. The methylated polysaccharides had the annexed properties.

	Main fraction of methyl derivative			
Glucomannan from	Yield (%) *	OMe (%)	$[\alpha]_D$ (in $CHCl_3$)	Sulphated ash (%)
L. umbellatum	56	44·7	−20° (*c*, 1·6)	0·3
L. henryii	34	44·0	−23° (*c*, 1·0)	1·2

* From the original glucomannan.

Fission of the Methylated Glucomannans.—Methanolysis was accomplished by boiling the methylated polysaccharide in methanolic hydrogen chloride (2% w/w) under reflux for 16 hr., and then the resultant methylglycosides were hydrolysed in aqueous N-hydrochloric acid at 95—100° for 16 hr. (for further details, see ref. 13). The yields of syrupy methyl-sugar mixtures were 90—95%.

[20] Brown, Halsall, Hirst, and Jones, *J.*, 1948, 27.
[21] Anderson, Greenwood, and Hirst, *J.*, 1955, 225.

Examination of the Methyl-sugar Mixtures.—Paper chromatograms [solvent (*c*)] indicated that each of the two mixtures consisted largely of tri-*O*-methylhexose (R_G 0·89), which moved at the same rate as the 2 : 3 : 6-tri-*O*-methyl derivatives of glucose and mannose. Small amounts of tetra-*O*-methyl- (R_G 1·00) and di-*O*-methyl-hexose (R_G *ca.* 0·6) were also present.

The sugar mixtures were fractionated by partition chromatography on hydrocellulose columns (28 × 4 cm.), with benzene–ethanol (4 : 1 v/v), nearly saturated with water, as the mobile phase. Butan-1-ol was added to this mixture to elute the di-*O*-methylhexoses.

The mixture of methyl-sugars (2·06 g.) from *L. umbellatum* gave the following fractions :

Fraction (1) (120) mg. was a syrup, containing compounds which gave two spots on the chromatogram, with R_G 1·00 and 0·89, in the approximate proportions of 3 : 1 respectively. After hydrolysis in N-hydrochloric acid at 100° for 5 hr., the proportions of the two substances had changed to *ca.* 2 : 1 respectively, indicating the presence of methyl tri-*O*-methylhexoside, but further hydrolysis effected no further change. Anions were removed from the hydrolysate with Amberlite resin IR-4B (carbonate form), the solution was evaporated, and the resultant sugar mixture (110 mg.) separated into the following two fractions on a large sheet-paper chromatogram, with solvent (*d*).

Fraction (1a) (65 mg.) [Found : OMe, 49·8. Calc. for $C_6H_8O_2(OMe)_4$: OMe, 52·5%] had R_G 1·00 and $[\alpha]_D$ +74° (*c*, 1·1). Demethylation of a portion (5 mg.) with hydrobromic acid (48% w/w; 1 c.c.) at 100° for 10 min. indicated that glucose was the parent sugar; mannose may have been present in much smaller amount, but could not be detected with certainty. The fraction was dissolved in ether–light petroleum (b. p. 60—80°) and, when seeded, gave a small crop of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, m. p. and mixed m. p. 85—87° [Found : OMe, 52·8. Calc. for $C_6H_8O_2(OMe)_4$: OMe, 52·5%]. The sugar (47 mg.) remaining in the mother-liquors was boiled in alcoholic solution with aniline (18 mg.) and yielded *N*-phenyl-D-glucopyranosylamine tetramethyl ether (25 mg.), which after recrystallisation from ethanol had m. p. and mixed m. p. 137—138° and $[\alpha]_D$ +235° (init. value; *c*, 0·2 in $COMe_2$).

Fraction (1b) (30 mg.) had R_G 0·89; it was combined with Fraction (2).

Fraction (2) (1·75 g.) [Found : OMe, 39·0. Calc. for $C_6H_9O_2(OMe)_3$: OMe, 41·8%] was a syrup, with $[\alpha]_D$ +19° (*c*, 2·5), which on the paper chromatogram with solvent (*c*) gave only one reddish-brown spot (R_G 0·89) with the *p*-anisidine hydrochloride reagent. A portion of this fraction (250 mg.) was boiled under reflux with a solution of aniline (100 mg.) in ethanol, and yielded *N*-phenyl-D-mannopyranosylamine 2 : 3 : 6-trimethyl ether (135 mg.), which after recrystallisation from ether–light petroleum (b. p. 40—60°) had m. p. 123°, raised to 125° on further recrystallisation, and $[\alpha]_D$ −152° (init. value; *c*, 0·6 in MeOH) ⟶ −39° (equil. value) (Found : N, 4·6. Calc. for $C_{15}H_{23}O_5N$: N, 4·7%). The mixture from which this derivative had crystallised was heated in N-sulphuric acid at 95° for 10 min., and the solution extracted continuously with chloroform. This gave a syrup (150 mg.) whcih was dissolved in ether and, when seeded, gave a very small crop (*ca.* 3 mg.) of 2 : 3 : 6-tri-*O*-methyl-D-glucose, m. p. and mixed m. p. 115—118°.

A portion (1·10 g.) of the fraction was oxidised with excess of bromine water in the usual way, and the resultant mixture of lactones examined on the paper chromatogram [solvent (*c*)] (cf. Abdel-Akher and Smith [22]). Two spots (R_G 0·92 and 1·00) were detected with ammoniacal silver nitrate, the former being the larger. The mixture of lactones was dissolved in ether, and when seeded the solution yielded 2 : 3 : 6-tri-*O*-methyl-D-mannono-γ-lactone (400 mg.), which after recrystallisation from ether had m. p. and mixed m. p. 79—80° and $[\alpha]_D$ +73° (init. value; *c*, 0·9) ⟶ +70° (90 hr.) [Found : OMe, 42·2. Calc. for $C_6H_7O_3(OMe)_3$: OMe, 42·3%]. The remaining lactone mixture (*ca.* 600 mg.) was chromatographed on large sheets of filter paper [solvent (*c*)], giving 2 fractions :

Fraction (2a) (210 mg.) consisted mainly (*ca.* 90%) of the compound with R_G 1·00, the remainder having R_G 0·92. It had $[\alpha]_D$ +54° (init. value; *c*, 1·1) ⟶ +44° (96 hr.). The syrup (190 mg.) could not be induced to crystallise, but when boiled in ethanol with phenylhydrazine (105 mg.) it gave crystalline 2 : 3 : 6-tri-*O*-methyl-D-gluconophenylhydrazide (105 mg.) which after recrystallisation from ethanol had m. p. 145—146° and $[\alpha]_D$ +18° (*c*, 1·0) (Found : N, 8·2. Calc. for $C_{15}H_{24}O_6N_2$: N, 8·5%).

Fraction (2b) (290 mg.) consisted mainly of the lactone (R_G 0·92) with a little of the gluconolactone (R_G 1·00). The former corresponded to 2 : 3 : 6-tri-*O*-methyl-D-mannono-γ-lactone, and when the fraction (80 mg.) was boiled in alcohol with phenylhydrazine (40 mg.) it yielded 2 : 3 : 6-tri-*O*-methyl-D-mannonophenylhydrazide, which crystallised from ethanol as the

[22] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.

monohydrate, m. p. 134—135° (m. p. 133—134° on admixture with an authentic specimen of m. p. 132°) and $[\alpha]_D$ −21° (*c*, 0·5) (Found: C, 52·2; H, 7·2; N, 7·9; loss of wt. on drying *in vacuo* at 110°, 4·6. Calc. for $C_{15}H_{24}O_6N_2,H_2O$: C, 52·0; H, 7·5; N, 8·1; H_2O, 5·2%). No other crystalline material was isolated from the mixture of phenylhydrazides.

The remainder of this fraction (2b) (210 mg.) was converted into the corresponding mixture of amides by dissolution in methanolic ammonia; after evaporation of the solution, the residual crystalline material (260 mg.) was dissolved in water (3 c.c.), and 0·6N-sodium hypochlorite (5 c.c.) added at 0°. Excess of sodium thiosulphate solution was added after 1 hr. at 0°, and the mixture then extracted continuously with chloroform. Evaporation of the chloroform gave crystalline material (80 mg.), which after 2 recrystallisations from acetone yielded colourless needles (25 mg.) of the cyclic *urethane* (III) derived from 2 : 3 : 6-tri-*O*-methyl-D-mannonamide, with m. p. 153° and $[\alpha]_D$ +37° (*c*, 1·0) [Found: C, 46·1; H, 7·4; N, 5·8; OMe, 38·7. $C_6H_8O_3N(OMe)_3$ requires C, 45·95; H, 7·2; N, 5·95; OMe, 39·6%]. The material from the chloroform extract was recombined (60 mg.) and dissolved in 0·3N-sodium hydroxide (10 c.c.), and the solution kept at room temperature for 48 hr. It was then neutralised with dilute sulphuric acid and evaporated to dryness, and the residue extracted with boiling ether. Evaporation of the ether gave a di-*O*-methylpentose (31 mg.) [Found: OMe, 33·3. Calc. for $C_5H_8O_3(OMe)_2$: OMe, 34·8%], $[\alpha]_D$ +30° (*c*, 1·2), which gave on the paper chromatogram one spot [R_G 0·71 in solvent (*c*)] which was purplish-brown with *p*-anisidine hydrochloride and indistinguishable from that of 2 : 5-di-*O*-methylarabinose. The sugar was oxidised with bromine water, but the derived lactone (18 mg.) did not recrystallise satisfactorily and accordingly was boiled in ethanol with phenylhydrazine (12 mg.). Evaporation of the ethanol gave a syrup which crystallised slowly; recrystallisation from ethanol afforded 2 : 5-di-*O*-methyl-D-arabono-phenylhydrazide as white needles, m. p. 162°.

Fraction (3) (40 mg.) [Found: OMe, 28·4. Calc. for $C_6H_{10}O_4(OMe)_2$: OMe, 29·8%] had $[\alpha]_D$ +56° (*c*, 0·9). A portion (5 mg.) on demethylation with hydrobromic acid (48% w/w; 1 c.c.) at 100° for 3 min. showed only glucose on paper chromatograms. On the paper chromatogram [solvent (*c*)] it gave a purple-brown spot (R_G 0·61) with *p*-anisidine hydrochloride, thus resembling 2 : 4-di-*O*-methylglucose, and differing from the 2 : 3-, 3 : 4-, and 4 : 6-isomers, which had R_G 0·67, 0·63, 0·54 and gave dark brown, light brown, and light brown spots respectively. When oxidised with bromine water in the usual way, the fraction (20 mg.) gave a syrupy lactone (16 mg.), $[\alpha]_D$ +77° (init. value; *c*, 0·8) ⟶ +57° (18 hr.) ⟶ +54° (48 hr.; equil. value). The lactone was converted, by treatment with methanolic ammonia, into a syrupy amide (20 mg.). The amide was dissolved in 0·6N-sodium hypochlorite (1 c.c.) and after 0·5 hr. at 0° excess of sodium thiosulphate solution was added, followed by sodium acetate (20 mg.) and semicarbazide hydrochloride (30 mg.). A slight precipitate (*ca.* 0·2 mg.), m. p. *ca.* 250°, had formed after 18 hr. at 0°. Under similar conditions, gluconamide (8 mg.) gave hydrazodicarbonamide (3·5 mg.), m. p. 255°.

The *L. henryii* mixture of methyl sugars (1·222 g.) gave the following fractions:

Fraction (1′) (20 mg.) was a syrup which on the paper chromatogram gave only one spot [R_G 1·00 in (*c*)], but hydrolysis [see under Fraction (1)] revealed that it contained *ca.* 20% of methyl tri-*O*-methylhexoside. The resultant mixture of tetra- and tri-*O*-methylhexoses was fractionated on a large sheet-paper chromatogram [solvent (*d*)] and the tetra-*O*-methylhexose (12 mg.) isolated. It had n_D^{20} 1·4560 and $[\alpha]_D$ +70° (*c*, 0·6). Demethylation of a portion (3 mg.) [see Fraction (1a)] showed glucose on the paper chromatogram, but mannose was not detected. Treatment of the tetra-*O*-methyl sugar (9 mg.) with aniline (5 mg.) in ethanol yielded *N*-phenyl-D-glucopyranosylamine 2 : 3 : 4 : 6-tetramethyl ether (5 mg.), m. p. and mixed m. p. 135—136°, $[\alpha]_D$ +240° (*c*, 0·6 in Me_2CO).

Fraction (2′) (1·140 g.) [Found: OMe, 40·7. Calc. for $C_6H_9O_3(OMe)_3$: OMe, 41·8%] was a syrup with $[\alpha]_D$ +19° (*c*, 1·6) which gave only one spot (R_G 0·89) on the paper chromatogram [solvent (*c*)]. Oxidation of a portion (500 mg.) with bromine water in the usual way yielded a mixture of two lactones [R_G 1·00 and 0·92 in solvent (*c*)]. This mixture was separated into two fractions by chromatography on large paper sheets with solvent (*c*):

Fraction (2′a) (120 mg.) consisted mainly of 2 : 3 : 6-tri-*O*-methyl-D-glucono-γ-lactone (R_G 1·00), $[\alpha]_D$ +52° (init. value; *c*, 2·0) ⟶ +42° (120 hr.). The lactone (70 mg.), when treated with phenylhydrazine (35 mg.) in boiling ethanol, gave 2 : 3 : 6-tri-*O*-methyl-D-glucono-phenylhydrazide (35 mg.) which after recrystallisation from ethanol had $[\alpha]_D$ +17° (*c*, 0·5) and m. p. 145°, undepressed on admixture with the specimen prepared from the *L. umbellatum* methyl-sugars.

Fraction (2′b) (295 mg.) consisted mainly of 2 : 3 : 6-tri-*O*-methyl-D-mannono-γ-lactone

(R_G 0·92) which crystallised when seeded. After recrystallisation from acetone–ether–light petroleum (b. p. 60—80°) it had m. p. and mixed m. p. 79—80° and $[\alpha]_D$ +70° (init. value; *c*, 1·2) ⟶ +68° (92 hr.). The material in the mother-liquors of the recrystallisation yielded 2 : 3 : 6-tri-*O*-methyl-D-mannonophenylhydrazide, which crystallised from ethanol as the monohydrate, m. p. and mixed m. p. 131—132°, $[\alpha]_D$ −18° (*c*, 0·5) [Found (on an anhydrous sample): N, 8·4; OMe, 28·4. Calc. for $C_{15}H_{24}O_6N_2$: N, 8·5; OMe, 28·4%].

Fraction (3′) (35 mg.) was a syrupy mixture of at least three di-*O*-methylhexoses [R_G 0·58—0·62 in solvent (*c*)] which were incompletely separated on the paper chromatogram. Demethylation of a portion with hydrobromic acid (48% w/w) for 3 min. at 100° showed both glucose and mannose on the paper chromatogram. It was not further examined.

Quantitative Analyses of the Methyl-sugar Mixtures.—The relative amounts of tetra-, tri-, and di-*O*-methylhexose in each methylated polysaccharide (*ca.* 20 mg. *L. umbellatum*; *ca.* 30 mg. *L. henryii*) were estimated, after methanolysis and hydrolysis as described above, by chromatographic separation on filter paper with solvent (*d*), and the separated methyl-sugars were then determined by alkaline hypoiodite.[23] 0·1N-Iodine (2 c.c.) in water (5 c.c.) with sodium hydroxide–sodium phosphate buffer (4 c.c.; pH 11·4) were used to oxidise the tetra- and the di-*O*-methyl sugars, and five times these amounts for the oxidation of the tri-*O*-methylhexoses. The oxidations were allowed to proceed for 18 hr. in the dark, and blanks were run concurrently. After acidification, the excess of iodine was titrated with 0·01N-sodium thiosulphate except in the case of tri-*O*-methyl sugars for which 0·1N-sodium thiosulphate was used. The results are summarised in the Table.

	Consumption of 0·01N-I_2 (c.c.)			Molecular ratios			
Glucomannan from	"Tetra"	"Tri"	"Di"	"Tetra"	"Tri"	"Di"	Average chain length
L. umbellatum ...	0·55, 0·60	13·1, 15·5	0·32, 0·43	1·0, 1·0	24, 26	0·6, 0·7	26, 28
L. henryii	0·49, 0·34	34·3, 24·8	1·24, 0·97	1·0, 1·0	70, 73	2·5, 2·8	74, 77

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[23] Hirst, Hough, and Jones, *J.*, 1949, 928; Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289.

35. *Degradative Studies on Peptides and Proteins. Part II.* Synthesis and Properties of 3-Benzoyl-1-phenyl-2-thiohydantoin.*

By D. T. ELMORE and P. A. TOSELAND.

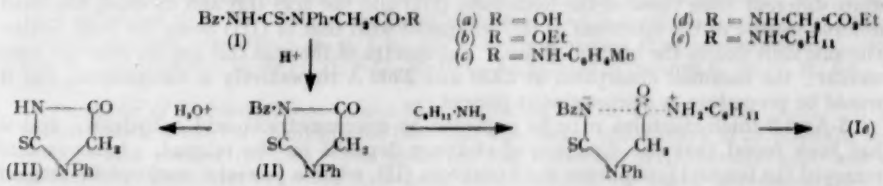
N-Benzoylthiocarbamoyl-*N*-phenylglycine (I*a*) and its ethyl ester (I*b*) and *p*-toluidide (I*c*), and *N*-benzoylthiocarbamoyl-*N*-phenylglycylglycine ethyl ester (I*d*), have been converted under suitable conditions of acid catalysis into 3-benzoyl-1-phenyl-2-thiohydantoin (II), a compound previously inadequately described by Douglass and Dains.[1] Hydrolysis of the 3-benzoyl group is brought about by aqueous acid, while *cyclo*hexylamine opens the ring to give *N*-benzoylthiocarbamoyl-*N*-phenylglycine *cyclo*hexylamide (I*e*).

IN Part I,[2] we mentioned that, under favourable conditions, acid-catalysed cyclisation and degradation of *N*-acetyl- and *N*-benzoyl-thiocarbamoyl-peptides and their derivatives may yield 3-acetyl- or 3-benzoyl-2-thiohydantoins as intermediates in the formation of the parent 2-thiohydantoin. The only 3-acyl-2-thiohydantoin previously described, so far as we are aware, is 3-benzoyl-1-phenyl-2-thiohydantoin (II).[1] It was claimed that *N*-benzoylthiocarbamoyl-*N*-phenylglycine (I*a*) and its ethyl ester (I*b*) were cyclised by sulphuric acid; no experimental details were recorded and the product was characterised only by nitrogen analysis and m. p. [it should be noted that the m. p.s of (I*a*), (I*b*), and (II) all lie within a few degrees]. Since other 3-acyl-2-thiohydantoins have been obtained only

* Part I, *J.*, 1954, 4533.

[1] Douglass and Dains, *J. Amer. Chem. Soc.*, 1934, **56**, 719.
[2] Elmore and Toseland, *J.*, 1954, 4533.

by use of careful techniques (forthcoming paper), and have been found to be highly reactive, we decided to repeat this work.



Methyl *N*-benzoyldithiocarbamate did not react with *N*-phenylglycine under the usual conditions;[2] this may be attributed to the electron-withdrawing behaviour of the *N*-phenyl group. An additional consequence of this effect is that this amino-acid probably shows little tendency to exist as dipolar ions in aqueous solution, although the p*K* of the imino-group does not appear to have been determined; as a result it is quite soluble in non-aqueous solvents. We found that *N*-benzoylthiocarbamoyl-*N*-phenylglycine (I*a*) and its ethyl ester (I*b*) could be prepared satisfactorily from benzoyl *iso*thiocyanate in acetone as described by Douglass and Dains.[1] The acid (I*a*) was converted into 1-phenyl-2-thiohydantoin (III) by hot 2*N*-sulphuric acid, no other product being detected by paper chromatography. When allowed to stand at room temperature in 80% sulphuric acid, the acid (I*a*) was unchanged while the ester (I*b*) was recovered partly as such and partly as acid. On the other hand, 98% sulphuric acid at room temperature cyclised the acid to 3-benzoyl-1-phenyl-2-thiohydantoin (II), but better yields were obtained by treatment of the acid or ester with cold trifluoroacetic acid. It was also observed that the ester was largely cyclised when stored in the solid state at room temperature for some weeks. Paper chromatography and determination of infrared spectra were indispensable analytical tools for following the course of these reactions.

3-Benzoyl-1-phenyl-2-thiohydantoin (II) was also obtained by stepwise degradation of peptides of *N*-phenylglycine.[2] It is interesting that peptides of *N*-phenylglycine may be synthesised without previous protection of the imino-group, a further consequence of the inappreciable formation of dipolar ions by this amino-acid. *N*-Phenylglycine *p*-toluidide and *N*-phenylglycylglycine ethyl ester were isolated in satisfactory yields (68 and 45% respectively) from the reaction of *N*-phenylglycine with *p*-toluidine and glycine ethyl ester respectively through the agency of tetraethyl pyrophosphite.[3] Benzoyl *iso*thiocyanate converted *N*-phenylglycine *p*-toluidide and *N*-phenylglycylglycine ethyl ester into their *N*-benzoylthiocarbamoyl derivatives (I*c* and *d*). The last two were not degraded in nitromethane or acetic acid saturated with dry hydrogen chloride,[4] but trifluoroacetic acid at room temperature gave good yields of the thiohydantoin. Trifluoroacetic acid has been found to be an excellent agent for procuring the cyclisation and degradation of other *N*-acylthiocarbamoyl-peptides, and, in view of its solvent properties for proteins,[5] may well find a wide use in this and the Edman method of stepwise degradation of peptides.

The structure of the thiohydantoin (II) has now been firmly established by complete microanalysis and by formation of this compound from the derivatives (I*c* and *d*). Further, its infrared spectrum is strikingly different from those of the acid (I*a*) and its ester and the hydrolysis product (III). In particular, this spectrum shows no band attributable to a N–H stretching mode; in addition, absence of hydrogen bonding results in all the bands' being very sharp. Two intense bands at 1730 and 1624 cm.$^{-1}$ are assigned to the heterocyclic and the exocyclic CO stretching frequency respectively. This designation is supported, first, by examination of the spectrum of the hydantoin (III), which possesses an intense band at 1725 cm.$^{-1}$ and, secondly, by the comparable spectral analysis of 1-acyl-2-thiohydantoins.[6] A very strong band at 1527 cm.$^{-1}$ in the spectrum of the compound

[3] Anderson, Blodinger, and Welcher, *J. Amer. Chem. Soc.*, 1952, **74**, 5309.
[4] Edman, *Acta Chem. Scand.*, 1950, **4**, 283; 1953, **7**, 700.
[5] Katz, *Nature*, 1954, **174**, 509.
[6] Randall, Fowler, Fuson, and Dangl, "Infra-Red Determination of Organic Structures," D. van Nostrand, Inc., New York, 1949, p. 177.

(II) is probably due to the N–C=S system.[7] The complexity of the spectrum precludes further analysis at this stage. The ultraviolet absorption of the benzoyl compound (II) is quite different from those of the hydantoin (III) and the acid (I*a*) and its ester, the most notable feature of the spectrum of (II) compared with that of (III) being the large bathochromic shift due to the benzoyl group. The spectra of the acid (I*a*) and its ester are very similar; the maximal absorption at 3330 and 3300 Å respectively is conspicuous, but it would be premature to discuss this at present.

3-Acyl-2-thiohydantoins may be regarded as unsymmetrical acid anhydrides, and it has been found that the direction of cleavage depends on the reagent. Aqueous acid removed the benzoyl group from the hydantoin (II), while a powerful nucleophilic reagent such as *cyclo*hexylamine effected cleavage of the 2-thiohydantoin ring, presumably by an S_N2 mechanism. Reaction occurred solely at $C_{(4)}$, to give *N*-benzoylthiocarbamoyl-*N*-phenylglycine *cyclo*hexylamide (I*e*); this compound was cyclised and degraded to the hydantoin (II) on treatment with trifluoroacetic acid. It is explicable why nucleophilic reagents do not attack $C_{(2)}$, since, although the $-M$ effect of sulphur is greater than that of oxygen, this is more than offset by the joint influence of $N_{(1)}$ and $N_{(3)}$. It is not clear, however, why the 3-acyl group is unaffected, particularly since 1-acyl-2-thiohydantoins are readily converted by basic reagents into the parent 2-thiohydantoins.

Experimental

Infrared spectra were measured in potassium bromide discs with a Grubb-Parsons double-beam spectrometer and a rock-salt prism.

N-Benzoylthiocarbamoyl-N-phenylglycine.—This *compound* was prepared by the general method of Douglass and Dains [1] and had m. p. 167—168° (Found: C, 61·0; H, 4·2; N, 9·0; S, 10·5. $C_{16}H_{14}O_3N_2S$ requires C, 61·1; H, 4·5; N, 8·9; S, 10·2%). The infrared spectrum contained the following bands: 3300, 3190, 3075, 2920, 1656, 1606, 1505, 1493, 1451, 1427, 1377, 1316, 1300, 1273, 1255, 1237, 1217, 1192, 1183, 1125, 1088, 1070, 1025, 1003, 986, 969, 933, 908, 832, 819, 799, 751, 710, 693 cm.$^{-1}$. Light absorption in EtOH: $\lambda_{max.}$ 3330 (ε 25,400), $\lambda_{min.}$ 2890 (ε 3200), $\lambda_{max.}$ 2420 Å (ε 16,300).

N-Benzoylthiocarbamoyl-N-phenylglycine Ethyl Ester.—Application of the above method to *N*-phenylglycine ethyl ester afforded the *N-benzoylthiocarbamoyl derivative*, m. p. 158—159° with softening at 125°, in good yield (Found: C, 62·9; H, 5·2; N, 8·2; S, 9·4. $C_{18}H_{18}O_3N_2S$ requires C, 63·1; H, 5·3; N, 8·2; S, 9·4%). Bands in the infrared spectrum were at 3300, 3020, 2980, 2920, 1744, 1644, 1606, 1591, 1481, 1459, 1435, 1382, 1328, 1302, 1279, 1231, 1207, 1182, 1128, 1114, 1094, 1074, 1032, 997, 932, 923, 909, 873, 847, 837, 797, 782, 755, 710, 703, 687 cm.$^{-1}$. Light absorption in EtOH: $\lambda_{max.}$ 3300 (ε 25,400), $\lambda_{min.}$ 2910 (ε 5300), $\lambda_{max.}$ 2430 Å (ε 17,600).

N-Phenylglycine p-Toluidide.—*N*-Phenylglycine (4·17 g.), *p*-toluidine (3·21 g.), and tetraethyl pyrophosphite (6·8 g.) were heated in diethyl hydrogen phosphite (30 c.c.) at 90—100° for 90 min. The cooled solution was poured into water (200 c.c.), and the precipitated solid (6·5 g.) was recrystallised twice from ethanol; then it had m. p. 170—171°. Meyer [8] reports m. p. 171—172° and Bischoff and Hausdörfer [9] record m. p. 165°.

N-Phenylglycylglycine Ethyl Ester.—*N*-Phenylglycine (3·02 g.), glycine ethyl ester hydrochloride (2·54 g.), triethylamine (2·08 g.), and tetraethyl pyrophosphite (4·5 g.) in diethyl hydrogen phosphite (25 c.c.) were heated at 90—95° for 40 min., cooled, and poured into water (200 c.c.). Precipitated solid (0·8 g.), m. p. 254—257° (decomp.) (presumably 2:6-dioxopiperazine), was collected, and the solution was extracted with ethyl acetate. The extract was dried and evaporated under reduced pressure; addition of light petroleum (b. p. 40—60°) caused *N*-phenylglycylglycine ethyl ester (3·1 g.) to crystallise; it had m. p. 84° (Wessely [10] reports m. p. 88°).

N-Benzoylthiocarbamoyl-N-phenylglycine p-Toluidide.—Benzoyl *iso*thiocyanate and *N*-phenylglycine *p*-toluidide in dry acetone afforded the *N-benzoylthiocarbamoyl derivative* (90%). Recrystallisation from ethanol gave a pale yellow product, m. p. 151° (Found: C, 68·6; H, 5·1; N, 9·9; S, 8·3. $C_{23}H_{21}O_2N_3S$ requires C, 68·5; H, 5·3; N, 10·4; S, 7·9%).

[7] Ref. 6, p. 5.
[8] Meyer, *Ber.*, 1875, **8**, 1152.
[9] Bischoff and Hausdörfer, *Ber.*, 1890, **23**, 1997.
[10] Wessely, *Z. physiol. Chem.*, 1925, **146**, 72.

N-Benzoylthiocarbamoyl-N-phenylglycylglycine Ethyl Ester.—Benzoyl *iso*thiocyanate and *N*-phenylglycylglycine ethyl ester were caused to react in dry acetone. The mixture was poured into water (100 c.c.), and the resultant yellow oil was extracted into chloroform. Addition of light petroleum (b. p. 40—60°) to the dried extract yielded *N-benzoylthiocarbamoyl-N-phenylglycylglycine ethyl ester* (55%), m. p. 118—119°; recrystallisation from aqueous ethanol raised this to 125° (Found: C, 59·7; H, 5·2; N, 10·3. $C_{20}H_{21}O_4N_3S$ requires C, 60·1; H, 5·3; N, 10·5%).

Behaviour of N-Benzoylthiocarbamoyl-N-phenylglycine and its Derivatives in Acids.—(i) *N*-Benzoylthiocarbamoyl-*N*-phenylglycine (300 mg.) was heated under reflux in 2N-sulphuric acid (20 c.c.) and ethanol (10 c.c.). The acid (I*a*), the hydantoin (III), benzoic acid, and an unidentified, ultraviolet-absorbing substance were detected by paper chromatography of aliquot parts withdrawn at intervals. After 5 hr., the hydantoin (III) (170 mg.) was isolated from the hydrolysate; it had m. p. and mixed m. p. 175°.

(ii) *N*-Benzoylthiocarbamoyl-*N*-phenylglycine in 80% sulphuric acid (cf. Douglass and Dains [1]) was unchanged after 2 days at room temperature. The ethyl ester under the same conditions was partly hydrolysed to the free acid.

(iii) *N*-Benzoylthiocarbamoyl-*N*-phenylglycine (2 g.) was dissolved in 98% sulphuric acid; the solution was kept at room temperature for 4 days and poured into water (500 c.c.). The resultant oil was extracted into ethyl acetate, and the extract was washed with 5% sodium hydrogen carbonate solution, followed by water, and dried. Addition of light petroleum (b. p. 40—60°) to the warm solution caused *3-benzoyl-1-phenyl-2-thiohydantoin* (0·84 g.) to separate as slightly purple crystals, m. p. 155—157° (Found: C, 64·9; H, 4·1; N, 9·2; S, 10·5. $C_{16}H_{12}O_2N_2S$ requires C, 64·8; H, 4·1; N, 9·5; S, 10·8%). Douglass and Dains [1] record m. p. 163° for their product of the same alleged structure. The infrared spectrum had bands at 2930, 2870, 1730, 1624, 1595, 1573, 1527, 1493, 1451, 1430, 1383, 1338, 1324, 1254, 1230, 1207, 1172, 1160, 1130, 1104, 1090, 1081, 1069, 1025, 1001, 951, 880, 824, 762, 722, 686, 678 cm.$^{-1}$. Light absorption in EtOH: $\lambda_{max.}$ 2980 (ε 14,600), $\lambda_{min.}$ 2930 (ε 14,200), $\lambda_{max.}$ 2870 (ε 14,800), $\lambda_{min.}$ 2760 (ε 13,600), $\lambda_{max.}$ 2590 Å (ε 20,600).

(iv) *N*-Benzoylthiocarbamoyl-*N*-phenylglycine *p*-toluidide and *N*-benzoylthiocarbamoyl-*N*-phenylglycylglycine ethyl ester were unaffected by dry hydrogen chloride in either nitromethane or acetic acid.

(v) All the foregoing *N*-benzoylthiocarbamoyl derivatives (I*a*, *b*, *c*, *d*) were cyclised in trifluoroacetic acid at room temperature. Experiments are summarised in the Table. The

Compound	Time (hr.)	Yield of (II) (%)	M. p.	Compound	Time (hr.)	Yield of (II) (%)	M. p.
I*a*	24	84	155—157°	I*c*	2	—	155—157°
I*b*	24	90	155—157	I*d*	0·25	92	156—157

product was isolated by pouring the reaction mixture into water. After recrystallisation from ethanol or dioxan, identity was established by determination of infrared spectra.

Reaction of 3-Benzoyl-1-phenyl-2-thiohydantoin with cycloHexylamine.—3-Benzoyl-1-phenyl-2-thiohydantoin (2 g.) in chloroform (20 c.c.) was warmed on the steam-bath for 10 min. with *cyclo*hexylamine (0·7 g.). The cooled solution was washed with dilute hydrochloric acid and evaporated under reduced pressure. The residue was crystallised from ethyl acetate–light petroleum (b. p. 90—120°). Pale yellow prisms (2·2 g.) of *N-benzoylthiocarbamoyl-N-phenylglycine cyclohexylamide* separated, having m. p. 167°, depressed on admixture with starting material (Found: C, 66·9; H, 6·3; N, 10·5; S, 7·9. $C_{22}H_{25}O_2N_3S$ requires C, 66·9; H, 6·4; N, 10·6; S, 8·1%). This compound in trifluoroacetic acid afforded 3-benzoyl-1-phenyl-2-thiohydantoin (65%).

Acid Hydrolysis of 3-Benzoyl-1-phenyl-2-thiohydantoin.—3-Benzoyl-1-phenyl-2-thiohydantoin (11 mg.) in ethanol (0·5 c.c.) and 2N-hydrochloric acid (0·5 c.c.) was heated at 100°; aliquot parts were removed at intervals, evaporated to dryness, and analysed by chromatography in butan-1-ol saturated with water and in benzene–acetic acid–water (1 : 1 : 1). After 2·5 hr., most of the starting material had been converted into 1-phenyl-2-thiohydantoin. Traces of two unknown substances were also detected.

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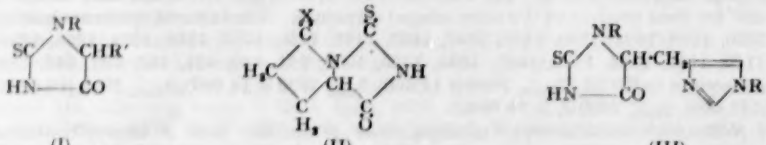
Staveley Research Laboratories,
The University, Sheffield, 10. [*Received, August 24th*, 1955.]

36. *Degradative Studies on Peptides and Proteins. Part III.* Synthesis of Some 2-Thiohydantoins as Reference Compounds.*

By D. T. Elmore, J. R. Ogle, and P. A. Toseland.

A number of 2-thiohydantoins have been synthesised as reference compounds for the recent method [1] of stepwise degradation of peptides from the end bearing a free amino-group.

The stepwise degradation of polypeptides from the end bearing a free amino-group by means of *N*-acyldithiocarbamates,[1] as well as the Schlack and Kumpf procedure [2] and its modifications [3, 4] from the end bearing a free carboxyl group, requires as reference compounds 2-thiohydantoins corresponding to all the amino-acids likely to be present in the polypeptide. Many of these have long been known; [5] those corresponding to histidine, arginine, ornithine, lysine, proline, methionine sulphone, cysteic acid, and *S*-methylcysteine have not been synthesised and characterised previously, although a few have been obtained as amorphous products which have not been analysed.[6] Various routes to these compounds were investigated and no one proved universally satisfactory. Improved methods for the synthesis of 2-thiohydantoins corresponding to glutamine and sarcosine have also been sought.



(I) (II) (III)

5-2′-Carbamoylethyl-2-thiohydantoin has recently been prepared in 45% yield by Swan [7] by the careful hydrolysis of the 1-acetyl derivative. We first examined the action of aqueous and ethanolic ammonia on 1-acetyl-5-2′-methoxycarbonylethyl-2-thiohydantoin (I; R = Ac, R′ = $MeO_2C{\cdot}[CH_2]_2$), which was in turn prepared in good yield from L-glutamic acid γ-methyl ester by the general method of Johnson and Nicolet.[8] Paper chromatography indicated a mixture of products. An alternative approach was suggested by the independent demonstrations by Rudinger [9] and Swan and du Vigneaud [10] that aqueous ammonia converted 5-oxo-1-toluene-*p*-sulphonylpyrrolidine-2-carboxylic acid into *N*-toluene-*p*-sulphonylglutamine. Similar treatment of 5′-oxopyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin (II; X = O) [11] gave a mixture. Replacement of aqueous by ethanolic ammonia, however, converted the compound (II; X = O) into the amide (I; R = H, R′ = $NH_2{\cdot}CO{\cdot}[CH_2]_2$) in excellent yield.

5-4′-Glyoxalinylmethyl-2-thiohydantoin (III; R = H) was readily obtained by acid hydrolysis in aqueous ethanol of 1-acetyl-5-(1-acetyl-4-glyoxalinylmethyl)-2-thiohydantoin (III; R = Ac).[7]

Crystalline pyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin (II; X = H_2) was forthcoming

* Part II, preceding paper.

[1] Elmore and Toseland, *J.*, 1954, 4533.
[2] Schlack and Kumpf, *Z. physiol. Chem.*, 1926, **154**, 125.
[3] Waley and Watson, *J.*, 1951, 2394; Tibbs, *Nature*, 1951, **168**, 910; Kjaer and Eriksen, *Acta Chem. Scand.*, 1952, **6**, 448; Kenner, Khorana, and Stedman, *J.*, 1953, 673; Baptist and Bull, *J. Amer. Chem. Soc.*, 1953, **75**, 1727.
[4] Dautrevaux and Biserte, *Compt. rend.*, 1955, **240**, 1153.
[5] Ware, *Chem. Rev.*, 1950, **46**, 403.
[6] Edward and Nielsen, *Chem. and Ind.*, 1953, 197.
[7] Swan, *Australian J. Sci. Res.*, 1952, **5**, *A*, 711.
[8] Johnson and Nicolet, *Amer. Chem. J.*, 1913, **49**, 197.
[9] Rudinger, *Chem. Listy*, 1954, **48**, 235, 244; *Coll. Czech. Chem. Comm.*, 1954, **19**, 365, 375.
[10] Swan and du Vigneaud, *J. Amer. Chem. Soc.*, 1954, **76**, 3110.
[11] Johnson and Guest, *Amer. Chem. J.*, 1912, **47**, 242.

from the acid-catalysed ring-closure of the non-crystalline *N*-benzoylthiocarbamoyl-L-proline ethyl ester, which was obtained by the interaction of benzoyl *iso*thiocyanate and L-proline ethyl ester. This thiohydantoin was previously obtained in an amorphous state (no analysis given) by Edward and Nielsen [6] using Johnson and Nicolet's method.[8]

5-3′-Guanidinopropyl-2-thiohydantoin (I; R = H, R′ = $NH_2{\cdot}C(:NH){\cdot}NH{\cdot}[CH_2]_3$), previously obtained in an amorphous state (no analysis given) by Edward and Nielsen,[6] was afforded crystalline by the acid-catalysed ring-closure of α-*N*-acetylthiocarbamoyl-L-arginine. The hydrochloride of 5-3′-aminopropyl-2-thiohydantoin (I; R = H, R′ = $NH_2{\cdot}[CH_2]_3$) was synthesised from DL-ornithine in a similar manner, although the intermediate α-*N*-acetylthiocarbamoyl-DL-ornithine could not be crystallised. This method, when applied to the synthesis of 5-4′-aminobutyl-2-thiohydantoin (I; R = H, R′ = $NH_2{\cdot}[CH_2]_4$) from L-lysine, gave a complex mixture from which the desired compound was separated, albeit in minute yield, by chromatography on powdered cellulose. Application of Johnson and Nicolet's [8] method to ε-benzyloxycarbonyl-L-lysine proved more satisfactory. Short hydrolysis of the oily intermediate 1-acetyl-5-4′-benzyloxycarbonylaminobutyl-2-thiohydantoin (I; R = Ac, R′ = $Ph{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}NH{\cdot}[CH_2]_4$) with dilute hydrochloric acid afforded the hydrochloride of the desired 5-4′-aminobutyl-2-thiohydantoin (I; R = H, R′ = $NH_2{\cdot}[CH_2]_4$) directly in modest yield. The previously reported "lysine 2-thiohydantoin," [4, 6] from its mode of preparation and its chromatographic behaviour, is probably 5-4′-acetamidobutyl-2-thiohydantoin (I; R = H, R′ = $Ac{\cdot}NH{\cdot}[CH_2]_4$).

1-Methyl-2-thiohydantoin (I; R = Me, R′ = H) was described by Komatsu [12] as a yellow crystalline solid, m. p. 214—215°, produced by heating a mixture of potassium thiocyanate and sarcosine ethyl ester hydrochloride in ethanol. This method, in our hands, gave a minute yield and we attribute this to the sluggish isomerisation of sarcosine ethyl ester thiocyanate to *N*-thiocarbamoylsarcosine ethyl ester.[13] In view of the recent discovery of sarcosine in ground-nut protein,[14] several other routes were examined. Although methyl *N*-acetyldithiocarbamate appeared to react with sarcosine in aqueous ethanol at pH 10, acid treatment of the gummy product failed to give identifiable material. *N*-Acetylthiocarbamoylsarcosine ethyl ester, obtained as a gum from the reaction between methyl *N*-acetyldithiocarbamate and sarcosine ethyl ester, and *N*-benzoylthiocarbamoylsarcosine ethyl ester, obtained as a crystalline solid from the reaction between benzoyl *iso*thiocyanate and sarcosine ethyl ester, both afforded 1-methyl-2-thiohydantoin, albeit in poor yield, when heated with dilute hydrochloric acid.

Stepwise degradation of polypeptides containing cystine residues is complicated by the presence of the disulphide bridge since, unless both amino-groups of cystine are free, no thiohydantoin is liberated. Thus Rovery, Fabre, and Desnuelle [15] found no *N*-terminal residue in chymotrypsinogen by the Edman procedure. Rupture of the disulphide bridge by oxidation with performic acid [16] is commonly employed and Bettelheim [17] found that oxidised chymotrypsinogen possessed one *N*-terminal cysteic acid residue, *i.e.*, one amino-group of cystine is free in chymotrypsinogen. Thus we have found it necessary to synthesise the 2-thiohydantoins corresponding to cysteic acid and methionine sulphone (since methionine is also oxidised by performic acid). The synthesis of 5-sulphomethyl-2-thiohydantoin (I; R = H, R′ = $HO_3S{\cdot}CH_2$) was accomplished through *N*-acetylthiocarbamoylcysteic acid. The thiohydantoin was found to be unstable in hot concentrated aqueous solution; cysteic acid was detected among the degradation products. For this reason cyclisation of the intermediate *N*-acetylthiocarbamoylcysteic acid was carried out in dilute solution and the time of reaction affording optimum yield was determined spectrophotometrically. 5-2′-Methylsulphonylethyl-2-thiohydantoin (I; R = H, R′ = $MeSO_2{\cdot}[CH_2]_2$) was easily made by Johnson and Nicolet's method.[8] An alternative method of cleaving cystine disulphide bridges involves reduction with sodium in liquid

[12] Komatsu, *Mem. Coll. Sci. Kyoto Imp. Univ.*, 1914, **1**, 69.
[13] Elmore, Toseland, and Tyrrell, *J.*, 1955, 4388.
[14] Haworth, MacGillivray, and Peacock, *Nature*, 1951, **167**, 1068.
[15] Rovery, Fabre, and Desnuelle, *Biochim. Biophys. Acta*, 1953, **12**, 547.
[16] Sanger, *Biochem. J.*, 1949, **44**, 126.
[17] Bettelheim, *J. Biol. Chem.*, 1955, **212**, 235.

ammonia followed by alkylation.[18] We have accordingly synthesised 5-methylthiomethyl-2-thiohydantoin (I; R = H, R′ = MeS·CH_2) from *S*-methylcysteine by Johnson and Nicolet's method.[8]

Experimental

1-Acetyl-5-2′-methoxycarbonylethyl-2-thiohydantoin.—A solution of γ-methyl hydrogen L-glutamate (2·4 g.) and ammonium thiocyanate (1·5 g.) in acetic anhydride (45 c.c.) and acetic acid (5 c.c.) was heated at 100° for 10 min., then poured into ice-water (250 c.c.). A yellow oil separated and was extracted into chloroform (40 c.c.). The extract was washed with 10% aqueous sodium hydrogen carbonate and water, dried ($CaSO_4$), and evaporated under reduced pressure to half its volume. Addition of light petroleum (b. p. 40—60°) caused the *thiohydantoin* (2·2 g.) to crystallise. Twice recrystallised from chloroform–light petroleum (b. p. 40—60°), it had m. p. 102° (Found: C, 44·1; H, 5·2; N, 10·7. $C_9H_{12}O_4N_2S$ requires C, 44·2; H, 5·0; N, 11·5%).

5-2′-Carbamoylethyl-2-thiohydantoin.—5′-Oxopyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin [11] (3 g.) was dissolved in saturated ethanolic ammonia (60 c.c.). After 5 min., the product (2·8 g.) separated, having m. p. 189°. Recrystallised from ethanol–light petroleum (b. p. 40—60°), it had m. p. 193° (Found: C, 38·8; H, 4·9; N, 22·0; S, 17·1. Calc. for $C_6H_9O_2N_3S$: C, 38·5; H, 4·9; N, 22·5; S, 17·1%). When aqueous ammonia was used, several products were shown to be present by paper chromatography.

5-4′-Glyoxalinylmethyl-2-thiohydantoin Hydrochloride.—1-Acetyl-5-(1-acetyl-4-glyoxalinylmethyl)-2-thiohydantoin (0·5 g.) was heated in ethanol–10N-hydrochloric acid (40 c.c.; 1 : 1) under reflux for 2 hr. On cooling, the *product* (0·26 g.) separated as pale yellow needles. Recrystallised from aqueous ethanol, it had m. p. 285—288° (decomp.) (Found: C, 36·1; H, 3·7; N, 24·3; S, 13·8. $C_7H_9ON_4SCl$ requires C, 36·1; H, 3·9; N, 24·1; S, 13·8%).

Pyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin.—L-Proline ethyl ester hydrochloride from L-proline (1 g.) was dissolved in dry acetone (15 c.c.) and treated with triethylamine (1·2 c.c.). After 15 minutes' shaking, the suspension was added to a solution of benzoyl *iso*thiocyanate [prepared by boiling a solution of ammonium thiocyanate (0·7 g.) and benzoyl chloride (0·7 c.c.) in acetone (15 c.c.) for 5 min.], and the mixture was boiled for a further 15 min., then poured into water. The oil which separated was extracted into ethyl acetate, and solvent was removed. The residual oil was heated in ethanol (30 c.c.) and 3N-hydrochloric acid (30 c.c.) for 3 hr. The white solid, which was deposited when the solution was concentrated under reduced pressure, was dissolved in ether, and the solution was washed with saturated aqueous sodium hydrogen carbonate, then water, and dried (Na_2SO_4). Removal of ether afforded the crystalline *thiohydantoin* (380 mg.), which, after recrystallisation from ethanol–light petroleum (b. p. 40—60°), had m. p. 161—163° (Found: C, 46·2; H, 5·3; N, 18·2. $C_6H_8ON_2S$ requires C, 46·1; H, 5·2; N, 17·9%).

α-N-Acetylthiocarbamoyl-L-arginine.—L-Arginine monohydrochloride (1·05 g.) was brought into reaction with methyl *N*-acetyldithiocarbamate (1·49 g.) in aqueous ethanol at pH 8·8. After removal of ethanol and extraction of excess of methyl *N*-acetyldithiocarbamate, the solution was evaporated to 10 c.c. and set aside at 0°. α-N-*Acetylthiocarbamoyl-L-arginine* (511 mg.) separated as its monohydrate and was recrystallised from water; it then darkened above 230° and finally melted at 252° with effervescence (Found: C, 36·5; H, 6·4; S, 10·9. $C_9H_{17}O_3N_5S,H_2O$ requires C, 36·8; H, 6·6; S, 11·0%).

5-3′-Guanidinopropyl-2-thiohydantoin Hydrochloride.—A solution of α-N-acetylthiocarbamoyl-L-arginine (200 mg.) in 2N-hydrochloric acid (2 c.c.) was heated under reflux for 1·5 hr. The solution was evaporated under reduced pressure to a syrup and then evaporated several times with ethanol. Final dissolution in ethanol and addition of ether afforded the crystalline *product* (150 mg.), m. p. 208—209° (effervescence) (Found: C, 33·4; H, 5·2; N, 27·4. $C_7H_{14}ON_5SCl$ requires C, 33·4; H, 5·6; N, 27·8%).

5-3′-Aminopropyl-2-thiohydantoin Hydrochloride.—A solution of DL-ornithine monohydrobromide (4 g.) in 50% aqueous pyridine (40 c.c.) was adjusted to pH 9 with triethylamine. After addition of methyl *N*-acetyldithiocarbamate (9·2 g.), the solution was heated under reflux for 3 hr., during which triethylamine (2 c.c.) was added in 6 portions. After 2 days at room temperature, the solution was filtered and concentrated under reduced pressure to an oil which was shaken with water and then extracted with benzene. The aqueous layer was acidified, extracted with three portions of ethyl acetate, then concentrated to a gum, which partially

[18] Gordon and du Vigneaud, *Proc. Soc. Exp. Biol. Med.*, 1953, **84**, 723.

solidified. The latter was dissolved in ethanol, and ether was added carefully to precipitate triethylamine hydrochloride (2 g.); further addition of ether precipitated a gum which was separated and heated in 5N-hydrochloric acid (25 c.c.) for 3 hr. Solvent was removed under reduced pressure; the residual gum was extracted with ethanol, and a small amount of insoluble material was removed. Addition of ether to the filtrate caused the *thiohydantoin hydrochloride* (860 mg.) to crystallize. It softened at 180° and was completely molten at 210° (Found: C, 32·7; H, 6·2; N, 19·5. $C_6H_{12}ON_3SCl,\frac{1}{2}H_2O$ requires C, 32·9; H, 6·0; N, 19·2%). Paper chromatography in three solvent systems and paper electrophoresis at pH 5·9 provided adequate evidence of its homogeneity.

5-4′-Aminobutyl-2-thiohydantoin Hydrochloride.—ε-*N*-Benzyloxycarbonyl-L-lysine (3·5 g.) and dry ammonium thiocyanate (2·1 g.) were heated under reflux for 20 min. in acetic anhydride (22·5 c.c.) and acetic acid (2·5 c.c.). The cooled mixture was poured into cold water (250 c.c.), and the resultant oil was extracted into chloroform. Solvent was removed under reduced pressure and the residue was heated in 3N-hydrochloric acid (50 c.c.) for 40 min. The solution was cooled and extracted with chloroform. The residual oil, after removal of chloroform, was further hydrolysed under similar conditions. The combined hydrolysates were evaporated to an oil under reduced pressure. The latter was extracted with ethanol, and the insoluble residue of the *thiohydantoin hydrochloride* (320 mg.) recrystallised from aqueous acetone; it then had m. p. 235—237° (Found: C, 37·4; H, 6·6; N, 19·0. $C_7H_{14}ON_3SCl$ requires C, 37·6; H, 6·3; N, 18·8%). Paper chromatography of the ethanol-soluble fraction indicated the presence of at least two substances, one of which was indistinguishable from the above thiohydantoin. The other was probably 5-4′-benzyloxycarbonylaminobutyl-2-thiohydantoin since, after treatment with 50% (w/v) hydrobromic acid in acetic acid at room temperature for 30 min. followed by precipitation with dry ether, paper chromatography in two solvents revealed the presence of a single substance having an R_F identical with that of 5-4′-aminobutyl-2-thiohydantoin hydrochloride. This was also obtained similarly to 5-3′-aminopropyl-2-thiohydantoin hydrochloride except that tri-*n*-butylamine replaced triethylamine. The resulting gum from 3·4 g. of lysine monohydrochloride was chromatographed on powdered cellulose (32 × 6·5 cm.) irrigated with *sec.*-butanol saturated with water, and a product (13 mg.) having m. p. 217—219° was separated. Although rather crude, this was indistinguishable by paper chromatography from the authentic thiohydantoin, gave a positive reaction with phosphotungstic acid, and had the expected light absorption.

N-Benzoylthiocarbamoylsarcosine Ethyl Ester.—The synthesis of this *compound* proceeded in 47% yield from sarcosine ethyl ester hydrochloride and benzoyl *iso*thiocyanate as described for the preparation of pyrrolidino(1′ : 2′-1 : 5)-2-thiohydantoin. Recrystallised from ethanol, it had m. p. 132° (Found: C, 55·9; H, 5·9; N, 10·3; S, 11·6. $C_{13}H_{14}O_3N_2S$ requires C, 55·7; H, 5·8; N, 10·0; S, 11·4%).

1-Methyl-2-thiohydantoin.—(*a*) *N*-Benzoylthiocarbamoylsarcosine ethyl ester (300 mg.) was heated in ethanol–10N-hydrochloric acid (1 : 1) for 2 hr. Solvents were removed under reduced pressure and the residue was shaken for 30 min. with sodium hydrogen carbonate solution. The insoluble residue, recrystallised from aqueous ethanol, had m. p. 224—226° (42 mg.) (Found: C, 36·5; H, 4·3. Calc. for $C_4H_6ON_2S$: C, 36·9; H, 4·7%).

(*b*) A solution of sarcosine ethyl ester (from 1 g. of hydrochloride) and methyl *N*-acetyldithiocarbamate (1 g.) in ethanol–ether (25 c.c.; 1 : 1) was kept at 37° for 7 days. Concentration of the solution precipitated unchanged methyl *N*-acetyldithiocarbamate which was removed. The filtrate was further evaporated to a gum, which was heated for 2 hr. with 2N-hydrochloric acid and left overnight at room temperature. The solution was extracted with ether, and the extract was dried and evaporated under reduced pressure. Fractional crystallisation of the residue from aqueous ethanol yielded 1-methyl-2-thiohydantoin (15 mg.), m. p. 217—219°, undepressed on admixture with the product from (*a*) and chromatographically indistinguishable from it.

(*c*) Sarcosine ethyl ester hydrochloride (1·5 g.) and potassium thiocyanate (1·5 g.) were heated in ethanol under reflux for 6 hr. Potassium chloride was removed and the filtrate was evaporated to a yellow oil, which was treated with 3N-hydrochloric acid for 2 hr. under reflux. Continuous ether-extraction of the solution afforded the crystalline thiohydantoin (17 mg.), m. p. 214—216°, chromatographically identical with the products from (*a*) and (*b*).

5-Sulphomethyl-2-thiohydantoin—A mixture of cysteic acid (3·4 g.) and methyl *N*-acetyldithiocarbamate (4·5 g.) in water (20 c.c.) and ethanol (20 c.c.) was kept at 40° and pH 8·5 for 24 hr., sodium hydroxide solution being added as necessary. The solution was evaporated under reduced pressure and extracted thoroughly with benzene. The aqueous layer was evaporated under reduced pressure to dryness, and the residual gum was dissolved in water (150 c.c.) and

passed through a column (30 × 2 cm.) of Dowex 50 resin (50—100 mesh) in the H^+-cycle. The column was washed with water 150 c.c.), and the combined percolate and washings were evaporated under reduced pressure to a gum. The latter in 2N-hydrochloric acid (150 c.c.) was heated for 1 hr. and then evaporated under reduced pressure to a white, deliquescent, crystalline *acid* (3 g.) (Found: C, 20·6; H, 3·6; N, 12·4. $C_4H_6O_4N_2S_2,H_2O$ requires C, 21·0; H, 3·5; N, 12·3%).

1-*Acetyl-5-2′-methylsulphonylethyl-2-thiohydantoin.*—DL-Methionine sulphone (4 g.) and ammonium thiocyanate (3·4 g.) were heated under reflux for 30 min. in acetic anhydride–acetic acid (20 c.c.; 9 : 1), then cooled and poured into water (100 c.c.), and the precipitated crystalline *product* (3·77 g.) was filtered off, washed with water, and dried. Recrystallised from dilute aqueous ethanol (charcoal), it had m. p. 195·5°, unchanged on further recrystallisation (Found: C, 36·6; H, 4·6. $C_8H_{12}O_4N_2S_3$ requires C, 36·6; H, 4·6%).

5-2′-Methylsulphonylethyl-2-thiohydantoin.—1-Acetyl-5-2′-methylsulphonylethyl-2-thiohydantoin (3 g.) was hydrolysed by hot 2N-hydrochloric acid (30 c.c.) for 1·5 hr. On cooling, the *product* (2·45 g.) crystallised and had m. p. 227—228° (decomp. after softening and darkening from about 200°). It recrystallised from water in cream-coloured needles, m. p. 228—229° (decomp. as before) (Found: C, 32·7; H, 4·4; N, 12·3; S, 28·4. $C_6H_{10}O_3N_2S_2$ requires C, 32·4; H, 4·5; N, 12·6; S, 28·8%).

5-Methylthiomethyl-2-thiohydantoin.—*S*-Methylcysteine (811 mg.) and ammonium thiocyanate (912 mg.) in 9 : 1 acetic anhydride–acetic acid (10 c.c.) were heated under reflux for 25 min. The mixture was cooled and poured into water. After being kept at 0° overnight, the crude product was collected and heated with 2N-hydrochloric acid (10 c.c.) for 1 hr. (hydrogen sulphide was copiously evolved). On cooling, an orange mass was precipitated; twice recrystallised from water (charcoal), it yielded colourless crystals (56 mg.) of *product*, m. p. 169—170° (Found: C, 34·4; H, 4·5; N, 15·3. $C_5H_8ON_2S_2$ requires C, 34·1; H, 4·6; N, 15·9%).

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37. *Specific Conductivity Measurements directly related to Solubilities with Special Reference to Calcium Sulphate (Anhydrite) Solutions.*

By W. M. MADGIN and D. A. SWALES.

The specific conductivity, κ, has been measured in aqueous calcium sulphate solutions, varying in concentration up to saturation with gypsum in the temperature range 20—50°. By considering rates of variation of conductivity with temperature for the different concentrations, the specific conductivities have all been converted into values corresponding to 20°. An equation has been derived to relate these adjusted values to concentration and hence to get solubilities directly from specific conductivity data for saturated solutions of anhydrite. This direct method has been applied to find solubilities of anhydrite in the range 20—35°.

HILL [1] casts considerable doubt on the trustworthiness of many of the solubility data for calcium sulphate (anhydrite), the chief cause of doubt being the absence of any real evidence of the existence of equilibrium in the saturated systems used although generally considerable time was given for this to occur. He comments on the dearth of information on the solubility of anhydrite at $<ca.$ 50°, and earlier [2] he concluded that it was in harmony with the van't Hoff mean valency rule that anhydrite should take many days in reaching saturation equilibrium. He also showed that, above 42°, gypsum has a greater solubility than anhydrite, gives constant reproducible solubilities, and does not decompose. Such

[1] Hill, *J. Amer. Chem. Soc.*, 1937, **59**, 2242.
[2] *Idem, ibid.*, 1934, **56**, 1072.

solutions are considered metastable. Hulett and Allen,[3] incidentally to some determinations of the solubility of gypsum by chemical analysis, measured the specific conductivity of saturated solutions at temperatures up to 100° and concluded that equilibrium was attained in no more than 1½ hours.

Posnjak [4] considers that disagreement among different authors is due to inefficient filtration when withdrawing samples of saturated solution for analysis, suspended particles being dissolved on dilution. He used both naturally occurring anhydrite and samples prepared by heating gypsum and concluded that the solubility varied with the origin of the anhydrite, a conclusion supported by Hill.[1]

In the present work an attempt was made to find solubilities of anhydrite directly from specific conductivities of the saturated solutions at 20—35°, by computation, and without chemical analysis. It was also hoped to find information about the time required to reach saturation equilibrium. Hill [1] concluded that the transition temperature for the change gypsum $\rightleftharpoons$ anhydrite is 42° ± 1° and that, although anhydrite should be metastable below 42°, it changes so slowly that steady and reproducible metastable solubilities can be measured. By using conductivity cells of known cell constants to contain saturated solutions, κ_t (t in °c) can be measured quickly and frequently without disturbing the saturating system by withdrawal of samples.

Conductivities of saturated calcium sulphate solutions at different temperatures will show variations due to changes in both concentration and ionic mobility, and a method is required to adjust κ_t values to one temperature only. Table 1 gives values for κ_t over a range of temperature, for seven unsaturated solutions. The seven linear graphs of conductivity against temperature have a common constant characteristic slope, A, and, with 20° as an arbitrary reference temperature, $\kappa_t = \kappa_{20} + (t - 20)A$ generally. The slope A varies with concentration and if its value could be found for any concentration then κ_{20} values for all solutions would be available. Plotting A against κ_{20} for the seven concentrations gives another linear graph, $A = b\kappa_{20} + a$ (Fig. 1), fitted by "least squares." The constants, found from the graph, are $a = 1{\cdot}743 \times 10^{-6}$ and $b = 1{\cdot}994 \times 10^{-2}$. Substitution for A in the foregoing equation for κ_t gives

$$\kappa_{20} = [\kappa_t - 1{\cdot}743 \times 10^{-6}(t - 20)]/[1 + 1{\cdot}994 \times 10^{-2}(t - 20)] \quad . \quad . \quad (1)$$

This equation covers the whole concentration range used and should enable any κ_t value to be converted into κ_{20} by which different solutions could be compared. Also the equation can be used to treat κ_t values for saturated solutions, measured at any temperature. A plot of κ_t against concentration at each experimental temperature appeared to give a parabola, an equation for which was found from our results. For seven different temperature the equations, of the form Concn. (wt.%) $(c) = A + B\kappa_t + D\kappa_t^2$, differed somewhat but correction of κ_t to κ_{20} by our equation reduced this disparity, and the mean of these corrected equations gave

$$c = -0{\cdot}0064 + 83{\cdot}26\kappa_{20} + 10{,}630\kappa_{20}^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Equation (2) is considered to be quite general and applicable to any solutions within the temperature range 20—50° and has been used to find solubilities of anhydrite in the range 20—35°. Anhydrite changes so slowly between 20° and 35° that steady and reproducible conductivities can be measured, solubilities found, and the time to reach saturation explored. Hulett,[5] experimenting only at 25°, also used a parabolic equation to connect κ_{25} with concentration but the expression is only of limited application. Roller,[6] studying saturated anhydrite solutions at 20°, reported a progressive rise in the conductivity to a maximum and, after a pause, a very slow decrease. The maximum was considered to be the true equilibrium value and the subsequent decrease was ascribed to slow hydration, causing a slight change in solubility.

Measurements of κ_t for certain calcium sulphate solutions led Kohlrausch [7] to propose

[3] Hulett and Allen, *J. Amer. Chem. Soc.*, 1902, **24**, 667.
[4] Posnjak, *Amer. J. Sci.*, 1938, **35**, 247.
[5] Hulett, *Z. phys. Chem.*, 1903, **42**, 577.
[6] Roller, *J. Phys. Chem.*, 1931, **35**, 1132.
[7] Kohlrausch, *Z. phys. Chem.*, 1908, **64**, 129.

an empirical expression for referring all values to a common temperature (18°), and he related these corrected values with concentration through infinite-dilution equivalent conductivity, an indirect procedure.

Experimental

Chemicals used were all at least of "AnalaR" purity. Anhydrite was prepared and dried by Hill's method;[8] analysis showed 100% purity.

Conductivity Cells.—Two cells (Fig. 2), designed specially for use with saturated solutions, had recesses to hold and protect the electrodes of thick platinum foil. The leads from the cell were connected through mercury to the electrical measuring circuit. The electrodes were cleaned and platinised by the methods of Popoff, Kunz, and Snow.[8] Each cell carried a tightly fitting rubber stopper with a ¼" steel ball-race bedded centrally. A Pyrex-glass paddle stirrer, held in the ball-race, rotated in a fixed position. The cells were immersed in a water-thermostat bath in aluminium holders.

Fig. 1.

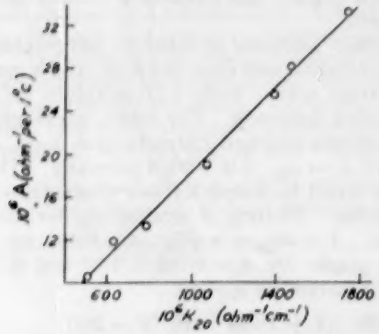
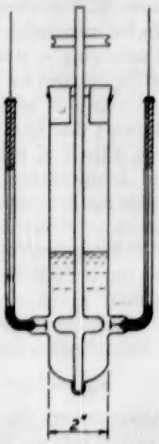


Fig. 2.



The thermostat was heated by a 250 w spiral immersion heater. A toluene–mercury temperature regulator incorporated a proportioning head, and the heater was coupled to an electronic relay; this gave temperature control better than ±0·01° at 25°.

Electrical Circuit.—Accurate resistance measurements were made with a Mullard bridge, type GM. 4140, extended by a four-decade inductance-free resistance, range 0—12,000 ohms by single units. An electron-beam indicator tube gave the balance point visually. Alternating current (1000 cycles sec.$^{-1}$) was supplied.

Cell Constants.—Jones and Bradshaw's methods[9] were followed in preparing the "demal"* potassium chloride solution used in finding the cell constants required to convert resistances into specific conductivities. Customary practice as to washing and rinsing was followed. The glass stirrers in the cells were stopped and raised while the resistance was measured; 20 mins. were allowed for equilibration of temperature before measurements of resistance.

Calcium Sulphate Solutions.—Seven unsaturated solutions were prepared from saturated gypsum solution and analysed by the oxalate–permanganate method. 150 c.c. of each solution were used in each conductivity cell. All seven solutions were similarly treated at 5° intervals up to 50°. Results (Table 1), corrected for distilled water, include densities, determined with pyknometers calibrated with distilled water. Thus compositions are expressible either by weight or volume. The distilled water had a specific conductivity between 2×10^{-6} and 4×10^{-6} mhos over the whole temperature range.

To extend the concentration range, saturated gypsum solutions have also been similarly examined. They were prepared in conductivity cells by adding 3 g. of gypsum to 150 c.c. of

* A "demal" solution was defined by Jones and Bradshaw[9] as one containing 1 mole of a salt per cubic decimeter of solution at 0°.

[8] Popoff, Kunz, and Snow, *J. Phys. Chem.*, 1928, **32**, 1056.
[9] Jones and Bradshaw, *J. Amer. Chem. Soc.*, 1933, **55**, 1780.

distilled water in a thermostat. Stirring was continuous, except when resistances were measured, and readings were continued until constant (≫*ca.* 3 hr.).

TABLE 1. *Conductivities* ($C = 10^6\kappa_t$, *ohm*$^{-1}$ *cm.*$^{-1}$) *and densities* (*d*) *of* $CaSO_4$ *solutions.*

$CaSO_4$ concn. (wt. %):	0·0332		0·0611		0·0689		0·1029	
Temp.	*d*	*C*	*d*	*C*	*d*	*C*	*d*	*C*
20·0°	0·99854	471·8	0·99924	740·4	0·99906	822·9	0·99930	1145
25·0	0·99750	522·9	0·99764	818·9	0·99770	904·7	0·99803	1258
30·0	0·99610	576·8	0·99626	890·5	0·99640	997·7	0·99656	1370
35·0	0·99459	630·2	0·99470	972·8	0·99465	1092	0·99500	1506
40·0	0·99254	684·8	0·99276	1056	0·99284	1184	0·99315	1638
45·0	0·99062	738·5	0·99122	1138	0·99123	1277	0·99135	1759
50·0	0·98848	793·3	0·98853	1216	0·98860	1367	0·98903	1881

$CaSO_4$ concn. (wt. %):	0·1312		0·1504		0·1620	
Temp.	*d*	*C*	*d*	*C*	*d*	*C*
20·0°	0·99964	1413	0·99976	1574	0·9993	1696
25·0	0·99849	1569	0·99863	1739	0·99874	1874
30·0	0·99704	1725	0·99708	1890	0·99732	2050
35·0	0·99554	1877	0·99563	2045	0·99574	2228
40·0	0·99349	2031	0·99366	2224	0·99372	2410
45·0	0·99166	2181	0·99215	2382	0·99194	2583
50·0	0·98898	2327	0·98953	2539	0·98960	2755

TABLE 2. *Conductivity* ($C_1 = 10^6\kappa_t$, $C_2 = 10^6\kappa_{20}$, *ohm*$^{-1}$ *cm.*$^{-1}$), *solubilities* (*S*), *and densities* (*d*) *of saturated gypsum solutions.*

Temp.:	20°	25°	30°	35°	40°	45°	50°
C_1	1966	2216	2433	2659	2882	3079	3268
C_2	1966	2006	2014	2026	2035	2025	2012
S (wt. %)	0·2040	0·2055	0·2073	0·2082	0·2102	0·2078	0·2048
d	1·00040	0·99915	0·99778	0·99620	0·99426	0·99244	0·99000

Solubilities (Table 2), found by direct analysis, are given, with κ values, the latter agreeing with those reported by Kohlrausch.[7] Samples for analysis were withdrawn through sintered-glass filters (porosity 4) (cf. Posnjak [4]). The solubilities at 45° and 50° are metastable for the solid phase gypsum as Hill [3] found at 45° and 60°.

From the entire range of conductivities, equation (2) was derived and applied to find solubilities of anhydrite from κ_t values for the corresponding saturated solutions without chemical analyses. Probably the equation is applicable outside the range 20—50°.

Solubility of Anhydrite.—Conductivities of saturated anhydrite solutions were measured as with saturated gypsum solutions and use of equations (1) and (2) gave solubilities (Table 3). The time to reach saturation equilibrium was shown when the conductivity reached a maximum (cf. Roller,[6] who reported the identical value for the conductivity at 20°).

TABLE 3. *Conductivities* (*C*), *solubilities* (*S*), *and time to reach equilibrium in saturated anhydrite solution.*

Temp.:	20°	25°	30°	35°
C_1	2637	2780	2897	3026
C_2	2637	1520	2401	2309
S (wt. %)	0·287	0·271	0·255	0·243
Time (hr.)	24	55	95	150

Comparison of results with those of other workers is possible only for individual temperatures. Hill,[1] using the analytical method, gives the same solubility at 35° as that now reported but, whereas he considered the time to reach equilibrium to be at least 28 days, we find that nowhere did it exceed 150 hr. Possibly such times are influenced by the efficiency of stirring. Posnjak [4] gives solubilities in good agreement with the present results but shows that results depend on the origins of the anhydrite used. For comparison, a sample of natural anhydrite (from Nottingham) was also used in the present work. It required a shorter time to reach equilibrium and gave a slightly lower solubility than the anhydrite prepared by Hill's method.[3] We regard the latter as the most satisfactory in giving anhydrite from which reproducible results are obtainable.

Hulett and Allen [3] found that a saturated solution containing solid gypsum attacked glass slightly at 50° and we find that with solid anhydrite in a saturated solution a slight and slow attack on glass occurs at about 40°.

The data for saturated gypsum (Table 2) show a maximum solubility at 40°, and the κ_{25} values run exactly parallel. This agrees with well-established results for the solubility of gypsum (see, *e.g.*, Hulett and Allen [9]).

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KING'S COLLEGE, NEWCASTLE UPON TYNE, 1. [*Received, June 23rd,* 1955]

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38. *Solutions of Alcohols in Non-polar Solvents. Part III.* The Viscosities of Dilute Solutions of Primary Alcohols in Benzene, Heptane, and cycloHexane.*

By L. A. K. STAVELEY and P. F. TAYLOR.

Measurements have been made at 20° C, with a precision of 0·01—0·02%, of the relative viscosities of dilute solutions in benzene, *cyclo*hexane, and heptane of the following normal primary alcohols: methanol to hexanol inclusive, octanol, and decanol. Only for heptane do the curves of specific viscosity against concentration fall regularly in the order of increasing molecular weights of the alcohols. Before the results can yield any information about changing configurations of the alcohol solute molecules with increasing chain length, allowance has to be made for the effect on the viscosity of the volume changes on mixing of solute and solvent. An attempt has been made to do this by supposing that for small volume changes the viscosity is to a first approximation a pure volume function. The corrected curves of viscosity against concentration for the solutions in *cyclo*hexane and benzene then fall in a regular sequence, but it seems that solutions of butanol, pentanol, and hexanol in benzene have smaller viscosities than might be expected from the behaviour of the other alcohols, which may be due to coiling of the molecules of these three alcohols in this solvent.

The results have also been discussed in relation to association of alcohols in non-polar solvents. The observed viscosity–concentration relations confirm a previous conclusion that the dimerisation stage is omitted. It seems probable that the first polymers formed are trimers.

PART I of this series (Staveley, Johns, and Moore, *J.*, 1951, 2516) dealt with measurements of the solubility and heat of solution of water in dilute solutions of alcohols in benzene. These measurements appeared to show that a change takes place in the interaction between the alcohol and benzene molecules on passing from butanol to pentanol, and it was tentatively suggested that in benzene solution the molecules of pentanol (and of higher alcohols) tend to adopt coiled configurations whereby the hydroxyl group is to some extent screened. Then (see Part II *) experiments were carried out on the volume changes on mixing of primary alcohols with benzene, heptane, and *cyclo*hexane, values being obtained for $\bar{V}_\infty$, the partial molar volumes of the alcohols in these three solvents at infinite dilution. In heptane, $\bar{V}_\infty$ increased by an almost constant amount from one alcohol to the next, whereas in benzene and *cyclo*hexane the increments per CH_2 group showed an alternation. These findings were not inconsistent with the possibility that the molecules with longer chains tend to adopt a coiled configuration in the solvents having cyclic molecules, but they could not be regarded as confirming this suggestion. They showed, however, that the volume relations between the members of homologous series in dilute solution depend on the nature of the solvent, and it was therefore thought worthwhile to examine viscosities, particularly since they can be measured very accurately and because, although our knowledge of the dependence of the viscosity of liquids on their structure is not as yet very detailed, the viscosities of dilute solutions must depend on the interaction between solution and solvent molecules; thus, if this interaction is affected by factors such as whether the number of carbon atoms in the alcohol molecule is odd or even, or whether the alcohol molecule tends to be coiled or not, these should in turn affect the viscosity. Admittedly

* Part II, Staveley and Spice, *J.*, 1952, 406.

the viscosity will in any case by influenced by the volume requirements of the solute molecules in the solution, and this will be considered in the Discussion.

Experimental

Owing to the association of alcohols in non-polar solvents, quite dilute solutions must be used to provide information relating to monomeric alcohol molecules. At room temperature, alcohols are effectively unassociated in benzene only at mole fractions $<0{\cdot}01$, and in heptane and *cyclo*hexane below the even smaller mole fractions of $\sim 0{\cdot}003$ and $0{\cdot}0015$ respectively (Wolf, *Trans. Faraday Soc.*, 1937, **33**, 179). Ideally, the viscosity measurements would have been made on solutions no more concentrated than these, but the viscosity differences between solution and solvent would then have been exceedingly small. It was therefore necessary to make measurements over a wider range of concentration, and to proceed by extrapolation to infinite dilution. For heptane and benzene, the range of mole fractions covered was $0{\cdot}005$ to $0{\cdot}03$, and in *cyclo*hexane $0{\cdot}002$ to $0{\cdot}025$. It was considered necessary to aim at an accuracy of $0{\cdot}02\%$ in the viscosity measurements. Two viscometers were used, of the Ostwald type constructed as described by Washburn and Williams (*J. Amer. Chem. Soc.*, 1913, **35**, 737). The total volume

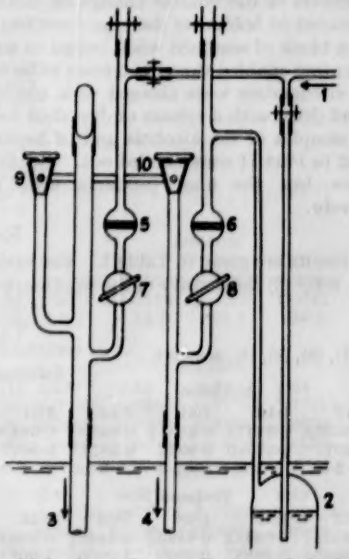


Fig. 1. *Fittings for each viscometer.* 1, Inlet for clean, dry, compressed air; 2, saturator; 3, to reservoir of viscometer; 4, to capillary of viscometer; 5, 6, sintered-glass filters; 7, 8, 9, 10, taps.

of liquid contained in each was about 66 c.c., of which about 25 c.c. discharged during a run through a capillary tube of internal diameter $\sim 0{\cdot}5$ mm., and length about 20 cm. According to the solvent and viscometer used, the flow times at 25° c varied from 17 to 45 min. These times were measured to 0·1 sec. with a hand-operated stop-watch. Usually the difference between the flow times for two consecutive runs agreed to within 0·2 sec. or better. Only very occasionally did they differ by as much as 0·5 sec. With every new solution or with an experiment with pure solvent, the first timed run was preceded by an untimed run.

In a series of experiments with any one alcohol in any one solvent, a known volume of pure solvent was introduced into one of the viscometers, and after temperature equilibrium had been reached the flow-time was determined, 2—3 measurements being made. Solutions of the alcohol were made up in the viscometer itself, beginning with the most dilute solution. To do this, a known weight of the pure alcohol was added from a weight pipette to the solvent in the reservoir of the viscometer *via* its wide limb. The liquids were mixed by bubbling dry dust-free air (saturated with solvent at the same temperature) down the capillary limb and up into the reservoir for 10—15 min. Then some of the solution was removed in a dropping pipette (read to 0·001 c.c.), so that the volume of the liquid in the viscometer would remain the same for each run. When the flow times for the solution so prepared had been measured, the next solution was made by the addition of more alcohol, and so on. Almost always, the complete series of experiments on any one alcohol in any one solvent was completed in a day.

Great care was taken to avoid contamination of the viscometers by dust, and in particular to see that the air used for mixing the solutions and also for pumping liquid from the reservoir of a viscometer to the bulb above the capillary was free from dust. Instead of taking air from the laboratory compressor, air was compressed by means of a hand-pump into a large glass bottle and maintained there at constant pressure. When an air-stream was required, it was taken from the bottle and passed successively through sulphuric acid, pumice soaked in sulphuric acid, phosphoric oxide, cellulose gauze, and a small sintered-glass filter. Fig. 1 shows the arrangement of these filters and of the necessary taps and connections at the top of each viscometer. The taps numbered 9 and 10 were necessary in order to put the spaces in the two tubes of the viscometer in direct communication before the start of each run. The rubber connections were made of new tubing which had been thoroughly washed. A strip-light just above the thermostat not only provided illumination but also (combined with suitable screening) kept the air at a temperature a little above that of the thermostat, thus eliminating the risk of the condensation of solvent from the air-stream in its passage from the saturator to the viscometer.

All experiments were carried out at 20° ± 0·005° c, this being the temperature at which the measurements of the volume change on mixing had previously been made. The viscometers were mounted on holders of the type described by Applebey (*J.*, 1910, 2000), which were screwed to a thick block of seasoned wood bolted to a rigid steel framework. This method of vibration-free mounting enabled the viscometers to be replaced always in exactly the same positions.

The viscometers were cleaned with concentrated nitric acid, distilled water, alcohol, and ether, and dried with a stream of dry, dust-free air.

The samples of the alcohols and of heptane used were those with which the experiments described in Part II were carried out. Benzene and *cyclo*hexane were purified in the same way as before, but the final products were slightly purer, having f. p.s 5·46° and 6·07° respectively.

Results

The results are given in Table 1. For each solution is recorded (1) the mole fraction x of the alcohol, $\times 10^2$ (2) the density of the solution, calculated from the figures given in Part II for the

Table 1.

For (1), (2), (3), (4), see text.

Solutions in heptane

Methanol

(1)	0·47	1·14	1·81	2·46	3·01
(2)	0·68369	0·68374	0·68383	0·68398	0·68409
(3)	0·9977	0·99545	0·9942	0·99315	0·9925
(4)	−2·35	−4·45	−5·6	−6·45	−6·9

Ethanol

(1)	0·75	1·10	1·62	2·14	2·63
(2)	0·68378	0·68386	0·68399	0·68414	0·68430
(3)	0·9973	0·99635	0·9962	0·99585	0·9958
(4)	−2·6	−3·45	− 3·4	−3·5	−3·45

Propanol

(1)	0·53	1·10	1·58	2·08	2·26
(2)	0·68387	0·68412	0·68436	0·68461	0·68489
(3)	0·99855	0·9988	0·9992	1·0000	1·0014
(4)	−1·2	−0·55	0·2	1·3	3·1

Butanol

(1)	1·05	1·54	2·02	2·50	2·91	3·44	3·92
(2)	0·6843	0·6846	0·6850	0·6853	0·6856	0·6860	0·6864
(3)	0·9997	1·0004	1·00185	1·00453	1·0082	1·0100	1·0132
(4)	0·6	1·7	3·7	6·8	11·0	13·5	17·1

Pentanol

(1)	0·52	1·04	1·55	2·11	2·53	2·90	3·37
(2)	0·68409	0·68454	0·68500	0·68554	0·68594	0·68629	0·68675
(3)	0·9999	1·00315	1·0056	1·0093	1·01245	1·0157	1·01935
(4)	0·5	4·4	7·5	12·0	15·8	19·5	23·9

Hexanol

(1)	0·50	1·15	1·69	2·21	2·76	3·35
(2)	0·68408	0·68485	0·68545	0·68602	0·68666	0·68734
(3)	1·0012	1·0060	1·0109	1·0164	1·0228	1·0302
(4)	1·8	7·7	13·5	19·9	27·2	35·7

Octanol

(1)	0·45	0·93	1·38	1·92	2·43	2·96
(2)	0·68421	0·68501	0·68567	0·68649	0·68729	0·68811
(3)	1·0037	1·0098	1·0169	1·0267	1·0361	1·0473
(4)	4·45	11·7	19·9	30·9	41·6	54·1

Decanol

(1)	0·48	0·99	1·48	2·01
(2)	0·68456	0·68551	0·68643	0·68745
(3)	1·0075	1·01925	1·0323	1·0471
(4)	8·8	21·95	36·45	52·85

TABLE 1. (*Continued*).

Solutions in benzene

Methanol

(1)	0·47	1·09	1·53	1·99	2·50
(2)	0·87888	0·87858	0·87837	0·87815	0·87791
(3)	0·9956	0·9903	0·9872	0·9843	0·98135
(4)	−4·7	−10·3	−13·6	−16·8	−20·0

Ethanol

(1)	0·53	1·10	1·64	2·11	2·63
(2)	0·87866	0·87820	0·87780	0·87745	0·87709
(3)	0·9954	0·9916	0·9883	0·9857	0·9836
(4)	−5·1	−9·4	−13·1	−16·2	−18·6

Propanol

(1)	0·50	1·00	1·50	2·02	2·56
(2)	0·87868	0·87827	0·87787	0·87746	0·87705
(3)	0·9971	0·9952	0·9929	0·9917	0·9907
(4)	−3·4	−5·7	−8·5	−10·2	−11·6

Butanol

(1)	0·51	1·04	1·51	2·02	2·47	2·95
(2)	0·87861	0·87811	0·8777	0·8772	0·8768	0·8764
(3)	0·9969	0·9947	0·9933	0·9929	0·9929	0·9938
(4)	−3·7	−6·5	−8·2	−9·3	−9·7	−9·3

Pentanol

(1)	0·57	1·09	1·63	2·15	2·67	3·24
(2)	0·87851	0·87798	0·87744	0·87694	0·87645	0·87593
(3)	0·9980	0·9970	0·9967	0·9975	0·9993	1·0013
(4)	−2·6	−4·2	−5·2	−4·9	−3·7	−2·3

Hexanol

(1)	0·53	1·04	1·69	2·10	2·63	3·29
(2)	0·87850	0·87779	0·87721	0·87679	0·87626	0·87563
(3)	0·9991	0·99915	1·0011	1·0040	1·0070	1·0116
(4)	−1·6	−2·3	−1·1	1·4	3·7	7·6

Octanol

(1)	0·51	1·04	1·56	2·02
(2)	0·87843	0·87775	0·87711	0·87657
(3)	1·0038	1·0087	1·0144	1·0226
(4)	3·0	7·1	12·1	19·7

Decanol

(1)	0·55	1·07	1·60	2·14
(2)	0·87827	0·87751	0·87674	0·87598
(3)	1·0072	1·0155	1·0259	1·0381
(4)	6·3	13·7	23·2	34·4

Solutions in cyclohexane

Methanol

(1)	0·34	0·83	1·23	1·62
(2)	0·77823	0·77814	0·77808	0·77802
(3)	0·9954	0·99015	0·9866	0·9844
(4)	−4·7	−10·1	−13·7	−16·0

Ethanol

(1)	0·18	0·49	0·78	1·04
(2)	0·77821	0·77807	0·77798	0·77791
(3)	0·9969	0·9924	0·9890	0·9870
(4)	−3·3	−7·9	−11·4	−13·5

Propanol

(1)	0·27	0·53	0·81	1·05	1·51
(2)	0·77822	0·77817	0·77813	0·77811	0·77808
(3)	0·9965	0·99295	0·9907	0·9889	0·9870
(4)	−3·6	−7·2	−9·5	−11·3	−13·2

Butanol

(1)	0·23	0·52	1·06	1·49	1·86
(2)	0·77823	0·77819	0·77821	0·77824	0·77826
(3)	0·9963	0·9931	0·9910	0·9902	0·9900
(4)	−3·8	−7·1	−9·1	−9·9	−10·1

Pentanol

(1)	0·29	0·57	1·15	1·70
(2)	0·77828	0·77828	0·77833	0·77842
(3)	0·9963	0·9940	0·9933	0·9935
(4)	−3·7	−6·0	−6·7	−6·4

Hexanol

(1)	0·51	1·01	1·54	2·01	3·14
(2)	0·77831	0·77839	0·77851	0·77864	0·77908
(3)	0·9946	0·9952	0·9978	1·0011	1·0107
(4)	−5·4	−4·6	−1·9	1·6	11·7

Octanol

(1)	0·29	0·54	0·86	1·16
(2)	0·77835	0·77843	0·77855	0·77868
(3)	0·9985	0·99935	1·0019	1·0062
(4)	−1·5	−0·5	2·2	6·7

Decanol

(1)	0·27	0·54	0·80
(2)	0·77840	0·77852	0·77864
(3)	1·0008	1·0040	1·0097
(4)	1·0	4·3	10·1

volume changes on mixing, in g./c.c. (3) the ratio of the observed time of flow for the solution to that for the pure solvent, each time being the mean of two, and sometimes three figures, (4) $10^3 \times$ the value of the specific viscosity $\eta_{sp.}$, where $\eta_{sp.} = (\eta_{soln.} - \eta_{solv.})/\eta_{solv.} = (\eta_{soln.}/\eta_{solv.}) - 1 = (\rho_{soln.}\ t_{soln.}/\rho_{solv.}\ t_{solv.}) - 1$, where ρ and t denote density and time of flow respectively. The values, 0·6837, 0·8701, and 0·7783 g./c.c., were chosen for the densities at 20° of heptane, benzene, and *cyclo*hexane respectively. Since it is the ratio of the density of a solution to that of the solvent which is important, the choice of slightly different values for the densities of the pure solvents has no significant effect on $\eta_{sp.}$.

In Figs. 2, 3, and 4 the values of $\eta_{sp.}$ are plotted against x, the mole fraction of the alcohol, for solutions in heptane, benzene, and *cyclo*hexane respectively. Data on solutions sufficiently dilute for comparison with our results exist only for propyl alcohol in benzene at 22° (Andrade

FIG. 2.

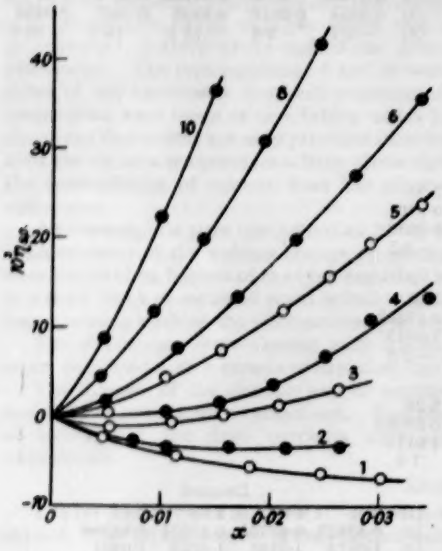


FIG. 3.

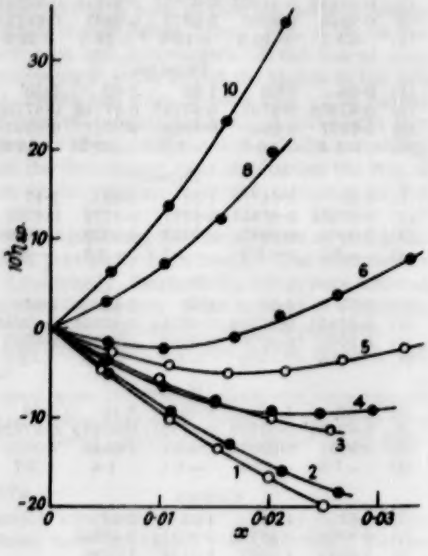
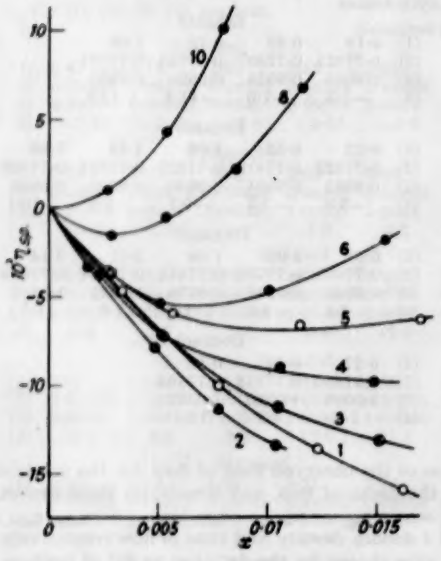


FIG. 4.



FIGS. 2, 3, and 4. *Values of $10^3\eta_{sp.}/x$, where $\eta_{sp.}$ = the specific viscosity, plotted against x, the molar fraction of the alcohol, for solutions in heptane (Fig. 2), in benzene (Fig. 3), and in* cyclo*hexane* (Fig. 4). *The number on each curve is the number of carbon atoms per molecule of the alcohol.*

and Spells, *J. Sci. Instr.*, **1932**, **9**, **316**; Spells, *Trans. Faraday Soc.*, **1936**, **32**, **530**). These results have been reproduced in Fig. 5, together with our own results for the same system at 20°.

Discussion

With heptane as solvent, only the lowest three (or possibly four) alcohols initially decrease the viscosity, and over the concentration range studied only the curves for ethanol and propanol (and perhaps butanol) show minima. For benzene solutions, the lower alcohols up to hexanol inclusive at first depress the viscosity, and the curves for butanol, pentanol, and hexanol show minima. So also, from Andrade and Spells's work, does the curve for propanol. For *cyclo*hexane, however, decanol is the only alcohol which does *not* reduce the viscosity at low concentrations, while the curves for the alcohols from pentanol to octanol show minima. These differences are to be correlated with the viscosities of heptane, benzene, and *cyclo*hexane at 20° which are in the ratio 1 : 1·59 : 2·35.

For a set of curves each showing a minimum in the viscosity, this minimum lies at a lower concentration the higher the molecular weight of the alcohol. For the lower alcohols, where the curves shown continuously decrease, minima will exist at higher concentrations, except for methanol in *cyclo*hexane, where the pure alcohol is less viscous than the hydrocarbon. The rapid change of slope of the curves and the appearance of the minima at such low molar fractions of alcohol show rather strikingly that association of the alcohol molecules begins at very low concentrations. Numerous attempts have been made to

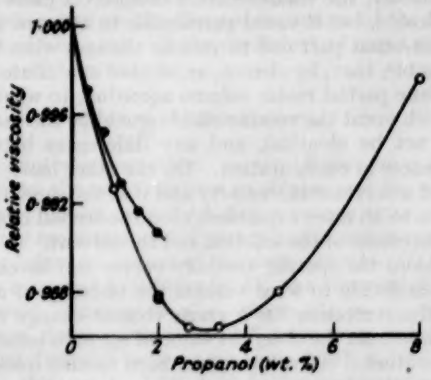


Fig. 5. *Plot of the relative viscosity of solutions of propanol in benzene against the weight percentage of the alcohol.*

●, *This work*, 20°; ○, *Andrade and Spells's results*, 22°.

relate viscosity (or fluidity) of binary liquid mixtures with the viscosities of the two pure components. It is doubtful if there is any value at all in attempting to do this for dilute solutions of alcohols in non-polar solvents where the alcohol begins as monomeric in extremely dilute solution, but rapidly forms polymers as the concentration increases, while the pure alcohol itself is very highly associated.

It will be seen from Fig. 2 that for heptane solutions the curve for any one alcohol lies between the curves for the two alcohols adjacent to it in the homologous series. But in benzene and *cyclo*hexane this is not always so, and in the initial influence of alcohols on the viscosities of these hydrocarbons we have a property which does not follow the sequence of the homologous series. For a property relating to the liquid state this is unusual. The effect is shown most strikingly for *cyclo*hexane solutions (Fig. 4), where the order of initial slopes is ethanol < butanol < propanol ~ methanol < pentanol < hexanol. For benzene solutions, propanol at first causes a smaller reduction in the viscosity than does butanol.

Table 2. *Values of A, the initial slopes of the curves obtained by plotting the corrected specific viscosity against molar fraction of alcohol.*

	Solvent				Solvent		
Alcohol	Heptane	Benzene	*cyclo*Hexane	Alcohol	Heptane	Benzene	*cyclo*Hexane
Methanol	−0·60	−2·04	−2·06	Pentanol ...	0·13	−1·09	−1·45
Ethanol	−0·48	−1·76	−1·90	Hexanol	0·33	−0·86	−1·15
Propanol	−0·34	−1·54	−1·76	Octanol	0·90	0·32	−0·44
Butanol	−0·16	−1·34	−1·56	Decanol	1·64	1·18	0·58

It is significant that these apparent anomalies can be related to the differences in the volume changes on mixing which were discussed in Part II, or, what amount to the same thing, to the apparent anomalies in the densities of dilute solutions of alcohols in the solvents concerned. Thus, if the densities given in Table 2 for solutions of alcohols in *cyclo*hexane are plotted against the molar fractions of alcohols, the relation between the curves is very much like that in Fig. 4, the order of the initial slopes of the density curves being in fact ethanol $<$ propanol $\sim$ butanol $<$ methanol $<$ pentanol. Alternatively, the point may be made in this way, that the relatively large effects of ethanol and butanol in reducing the viscosity of *cyclo*hexane are due partly to the fact that they mix with this hydrocarbon with a larger volume increase than the other alcohols, while this volume increase is least for methanol, which therefore has a relatively small effect in decreasing the viscosity. Likewise, in benzene solution, the inversion in the sequence of propanol and butanol is due to the fact that, at low alcohol concentrations, propanol mixes with a smaller volume increase than either ethanol or butanol, which leads to a smaller reduction in the viscosity with propanol.

Until allowance has been made for volume effects, therefore, it seems impossible to decide whether the viscosity results give any indication that the alcohol molecules adopt different configurations depending on the length of their chain and the nature of the solvent. Admittedly, the volume effects themselves must depend on the configuration adopted by the alcohol, but it seems permissible to attempt to separate from the overall effect on the viscosity that part due to volume changes when the solution is formed. For example, it is possible, that, by chance, an alcohol in a dilute solution in which it is all monomeric has the same partial molar volume according to whether the molecules are straight or coiled, in which event the volume effects would be the same. But the viscosities for the two cases need not be identical, and any differences between them could be ascribed solely to differences in configuration. On the other hand, if coiling of the solute molecules in itself caused a decrease in viscosity and if at the same time this coiling caused the solvent–solute system to be more expanded, then the second effect would enhance the difference between the viscosities of the solution and the solvent.

Before the specific viscosity curves can be corrected for volume effects, however, we have to decide to what volume the viscosity of any solution is to be corrected, and then how the correction for a given volume change is to be made. For the first one might calculate from the observed value of $\eta_{sp.}$ for a solution at 20° what $\eta_{sp.}$ would be at the same temperature if the solution had been formed from the two liquids with no volume change. This implies, however, that the pure alcohols themselves are a suitable standard for normal behaviour. Actually, they are highly associated, probably into chains of indefinite length, while we are concerned with drawing conclusions, from the properties of dilute solutions in which association is only beginning, about the properties of extremely dilute solutions in which the alcohol is all monomeric. (We may note that, in fact, for the lower alcohols at least, both the viscosities and the molar volumes of the pure alcohols seem to show a slight but definite alternation.) A better choice seems to be to estimate what the viscosity of a given solution would be at the volume which it would have if it had been formed with the same volume change per mole of alcohol as that for the same alcohol on forming a very dilute solution in heptane at the same temperature. The reasons for choosing heptane are: (1) it was shown in Part II that the increments per CH_2 group in the partial molar volumes of the alcohols at infinite dilution are constant within experimental error in heptane (apart from the first step, methanol to ethanol), which is not so for benzene and *cyclo*hexane; (2) as already pointed out, the curves of $\eta_{sp.}$ against alcohol concentration fall in the normal sequence of the alcohols in this solvent, but not in the other two; (3) like the alcohols, it has a straight chain. The second question, namely, how the viscosity is to be corrected for a given volume change, must also be answered rather arbitrarily, since it is known that the viscosity of a liquid is not, in fact, a pure volume function. Nevertheless, it appears that at least at low pressures, and for unassociated liquids, the changes in viscosity brought about by temperature changes and by changes in pressure (if these are not too great) are largely due to the associated volume changes. Unfortunately, there are no data on the effect of compression on the viscosity of heptane and *cyclo*hexane at 20°, and the only

datum for benzene is that provided by the early work of Warburg and Sachs (*Wied. Annalen*, **1884**, **22**, 518). We may use this as follows to examine how far changes in the viscosity of benzene are determined by volume changes alone. If benzene is cooled from 20° to 19°, the percentage increase in viscosity is 1·54. If benzene at 20° is compressed until its volume is the same as it would be at 19°/1 atm., then according to Warburg and Sachs's results the viscosity would increase by 1·25%. Thus the change in viscosity with temperature is largely but not completely determined by the volume change. However, in view of the absence of information about the effect of pressure on the viscosity of heptane and *cyclo*hexane, the only consistent way in which we can correct for volume effects is by making use of the effect of temperature on the viscosity. The following procedure has, therefore, been adopted.

The actual volume of a solution consisting of $(1 - x)$ moles of solvent and x moles of an alcohol is $V = (1 - x)V_0 + xV_a + xv$, where V_0 and V_a are the molar volumes of pure solvent and alcohol respectively, and v is the observed volume increase on mixing per mole of alcohol. We wish to know the amount $\delta\eta$ by which the observed viscosity of this solution would change if its volume was altered to $(1 - x)V_0 + xV_a + xv_0$, where v_0 is the volume increase on mixing of one mole of the same alcohol with an infinite amount of heptane. That is, we wish to estimate the change $\delta\eta$ in the viscosity if the volume V of one mole of the actual solution is increased by δV, where $\delta V = x(v_0 - v)$. As already indicated, we propose to do this by combining data on the thermal expansion of the liquid with those on the temperature coefficient of viscosity. If the coefficient of expansion of the solution is α, then $\alpha = (1/V)(\partial V/\partial T)_p$, and if we let

$$\beta = \frac{1}{\eta}\left(\frac{\partial \eta}{\partial T}\right)_p, \text{ then } \frac{\delta\eta}{\eta} = \frac{\beta\delta V}{\alpha V} = \frac{\beta}{\alpha V}x(v_0 - v).$$

In the absence of information about the solutions themselves, we shall adopt for α and β the values for the three pure solvents. As the solutions are so dilute, and as we are dealing with a correction term, this approximation cannot involve a serious error. It is also sufficiently accurate to put $V = V_0$, the molar volume of pure solvent, and to regard η in the above equation (the viscosity of the solution) as that of the pure solvent. If, therefore, one mole of the actual solution were increased in volume by δV, the observed specific viscosity of the actual solution, $\eta_{sp.}$, would increase to $\eta'_{sp.}$, where $\eta'_{sp.} = \eta_{sp.} + \delta\eta/\eta$. The following values of α and β for the three solvents at 20° have been estimated from the data in the International Critical Tables: for benzene, $\alpha = 1{\cdot}237 \times 10^{-3}$, $\beta = -1{\cdot}54 \times 10^{-3}$; for heptane, $\alpha = 1{\cdot}238 \times 10^{-3}$, $\beta = -1{\cdot}16 \times 10^{-3}$; for *cyclo*hexane, $\alpha = 1{\cdot}162 \times 10^{-3}$, $\beta = -1{\cdot}70 \times 10^{-3}$. The necessary values of v_0 and v were taken from the results given in Part II.

The values of $\eta'_{sp.}$ obtained in this way proved to be quadratic functions of x, the mole fraction of the alcohol, the relation being of the form $\eta'_{sp.} = Ax + Bx^2$. We are concerned with the values of A, the initial slope of the corrected curve. The slope A, $= (d\eta'_{sp.}/dx)_{x\to 0}$, is therefore analogous to the quantity sometimes called the intrinsic viscosity. The slope A was evaluated by plotting $\eta'_{sp.}/x$ against x, drawing the best straight line through the points and extrapolating to $x = 0$. The values of A so obtained are given in Table 2, and are plotted in Figs. 6 and 7 against the number of carbon atoms in the alcohol molecules. It will be seen that, for heptane, the values of A fall on a smooth curve. For this particular solvent this would still be true even if A were calculated from $\eta_{sp.}$ itself. For *cyclo*hexane, however, the corrections for volume effects have made a radical alteration, for, as shown in Fig. 6, for this solvent also the A values are a smooth function of x, within the limits of experimental error. This is in striking contrast to the relation between the observed relative viscosity–concentration curves of Fig. 4. We may therefore say that there is no evidence from these viscosity studies that in heptane solutions any of the alcohols has an abnormal influence on the viscosity which can be attributed to configurational effects, and the same appears to hold for *cyclo*hexane solutions after allowance has been made for volume effects.

With benzene, however, the position is rather different. It will be seen from Fig. 7 that the points for butanol, pentanol, and hexanol fall below the curve through the other

points. Fortunately, for this solvent the plots of $\eta'_{sp.}/x$ against x, from which the values of A were obtained, give good straight lines of relatively small slope, and we do not think that the failure of the points in Fig. 7 to conform to a smooth curve can be ascribed to experimental error. It therefore appears that when these alcohols are introduced into benzene in the monomeric form they reduce the viscosity more than would be expected from the behaviour of the alcohols which precede and follow them in the homologous series, the effect persisting even when allowance has been made for volume changes. It may be significant that it is for these alcohols that coiling of the molecules might be expected to screen the hydroxyl group, which is known to be capable of quite strong interaction with benzene molecules. It is true that in Part I the coiling of the alcohol molecules in solution was suggested as a possibility which might apply to pentanol and octanol, but not to butanol, to account for the different effects of butanol as compared with the other two alcohols on the heat of solution of water in the medium: whereas here, from Fig. 7, it might be said that, if butanol, pentanol, and hexanol are abnormal in their behaviour, then

FIG. 6. FIG. 7.

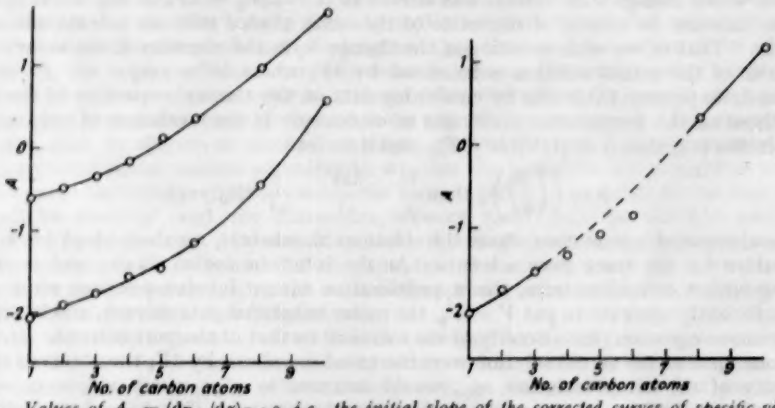


FIG. 6. *Values of* A, $= (d\eta_{sp.}/dx)_{x\to 0}$, *i.e., the initial slope of the corrected curves of specific viscosity against molar fraction of alcohol, plotted against the number of carbon atoms per molecule of the alcohol.*
Upper curve, *solutions in heptane.* Lower curve, *solutions in* cyclo*hexane.*

FIG. 7. *Corresponding plot to those in Fig. 6 for solutions in benzene.*

octanol is normal. But there is no reason, in comparing a series of dilute solutions where the solutes have flexible molecules capable of a variety of configurations, to suppose that the effect of this flexibility on the thermodynamic properties is necessarily a guide to its influence on a property such as viscosity.

We shall finally consider the bearing of our results on the problem of the association of alcohol molecules in non-polar solvents, and we shall show that they support the belief that in this association the dimer stage is omitted, a conclusion first reached from spectroscopic studies (Kreuzer and Mecke, *Z. phys. Chem.*, 1941, **49**, *B*, 309; Mecke and Nückel, *Naturwiss.*, 1943, **21**, 248; Hoffmann, *Z. phys. Chem.*, 1943, **53**, *B*, 179). If we suppose that the association begins by n monomer molecules A aggregating to a polymer A_n, then the equilibrium constant K for the reaction $nA \rightleftharpoons A_n$ is given by $K = \alpha/n(1-\alpha)^n c^{n-1}$, where α is the fraction of the alcohol associated, and c is the total concentration of the alcohol, expressed in moles/l. as if it were wholly present as monomer. In the early stages of the association we may write

$$(1-\alpha)^n \approx 1 - n\alpha \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and with this approximation we have

$$\alpha = Knc^{n-1}/(1 + Kn^2c^{n-1}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

At the low solute concentrations involved here, we may suppose that the monomer and polymer alter the viscosity of the solvent by amounts proportional to their respective

concentrations (with, of course, different proportionality factors for the two species). Since the monomer concentration is $(1 - \alpha)c$, while the polymer concentration is $\alpha c/n$, we have

$$\eta_{soln.} = \eta_{solv.} + P(1 - \alpha)c + Q\alpha c/n$$

where P and Q are constants for a given alcohol and a given solvent at a given temperature. Hence

$$\eta_{sp.} = (\eta_{soln.} - \eta_{solv.})/\eta_{solv.} = Dc + E\alpha c,$$

where $$D = P/\eta_{solv.}, E = \left(\frac{Q}{n\eta_{solv.}} - \frac{P}{\eta_{solv.}}\right).$$

Substituting for α from equation 2 above, we have

$$\eta_{sp.} = Dc + EKnc^n/(1 + Kn^2c^{n-1})$$

Rearrangement of this last equation gives

$$c^n/(\eta_{sp.} - Dc) = (1 + Kn^2c^{n-1})/EKn$$

Since the mole fraction x of the alcohols never much exceeds 0·02, we may replace c by x. The value of D is then the initial slope of the curve of $\eta_{sp.}$ against x, and it can be obtained by drawing tangents at the origin to the curves of Figs. 2, 3, and 4. Subject to the validity of the approximation (1) above, we should find that, if the association begins by dimerisation ($n = 2$), then a plot of $x^2/(\eta_{sp.} - Dx)$ against x should be linear. If trimers are the first aggregates formed, a plot of $x^3/(\eta_{sp.} - Dx)$ against x^2 should be linear, while for tetramers this should be true of a plot of $x^4/(\eta_{sp.} - Dx)$ against x^3. It should be noted that, whichever possibility actually applies, the corresponding plot should have a positive slope.

In order to apply these criteria of association, we have selected, for each of the three solvents, the five " best " curves of each of Figs. 2, 3, and 4, *i.e.*, those for which the experimental points conform most closely to the smooth curves drawn through them. With the curves rejected for this purpose, the uncertainty in the slope of the initial tangent was thought to be too large. The three plots corresponding to dimers, trimers, and tetramers were then carried out for each of the fifteen systems selected. For twelve of these systems, so far from the plot of $x^2/(\eta_{sp.} - Dx)$ against x being linear, the values of the former quantity did not even increase continuously with x. For none of the other three systems did this plot give the best straight line. We may therefore conclude that polymerisation does not begin by dimerisation in heptane, benzene, or *cyclo*hexane. For ten of the fifteen systems, the plot for which the points conformed most closely to straight lines was that corresponding to trimerisation. For the other five systems it was not possible to decide whether the results favoured association into trimers rather than tetramers. The value of the quantity $(\eta_{sp.} - Dx)$, especially at low concentrations, is rather sensitive to the slope of the initial tangent to the curve. But at least it is fair to say that our results confirm the view that the dimerisation stage is omitted in the association, and on the whole make it probable that, in all three solvents, the first aggregates formed are trimers.

Confirmation of the first of these conclusions comes from a consideration of Fig. 5, in which Andrade and Spells's results for propanol in benzene are plotted. The curve here suggests that the aggregate into which the propanol first associates increases the viscosity of the solution very considerably. If this aggregate is a dimer, it would be a molecule of about the same size and mass as the monomer of hexanol, and might be expected to have much the same effect as the latter on the viscosity. Since our results show that the monomer of hexanol reduces the viscosity of benzene, the inference is that the polymer into which propanol first associates is larger than a dimer.

We are grateful to Professor J. H. Wolfenden for advice on the construction and mounting of viscometers.

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39. *The Latent Heat of Vaporization and the Thermochemistry of Ethyl Nitrate.*

By Peter Gray, M. W. T. Pratt, and M. J. Larkin.

In order to correlate the existing thermochemical data for ethyl nitrate, reliable latent-heat data are required. To provide these the vapour pressure of ethyl nitrate has been measured from 0° to 68°. The results obtained, combined with existing low-temperature work, can be represented by the Antoine equation: $\log_{10} p$ (mm.) $= 7{\cdot}145 - 1329/(t° \text{C} + 224{\cdot}0°)$. The latent heat of vaporization (kcal. mole^{-1}) at 25° is 8·7; at the b. p. (87·7°/760 mm.) it is 8·1. The Trouton constant (cal. deg.$^{-1}$ mole^{-1}) is 22. The standard enthalpy of formation (kcal. mole^{-1}) at 25° of liquid ethyl nitrate is −45·7 and of gaseous ethyl nitrate is −37·0.

Three experimental determinations have been made from which the enthalpy of formation of ethyl nitrate may be calculated. The first was made in 1876 by Berthelot,[1] who measured directly the heat liberated during the esterification of liquid ethanol with pure nitric acid:

$$\text{EtOH(l)} + \text{HNO}_3\text{(l)} \longrightarrow \text{EtO·NO}_2\text{(l)} + \text{H}_2\text{O(l)};\ \Delta H = -6{\cdot}2 \text{ kcal. mole}^{-1}$$

The second was made in 1886 by Thomsen,[2] who measured the heat of combustion of gaseous ethyl nitrate:

$$\text{EtO·NO}_2\text{(g)} + 1{\cdot}75\text{O}_2 \longrightarrow 2\text{CO}_2 + 2{\cdot}5\text{H}_2\text{O(l)} + 0{\cdot}5\text{N}_2;\ \Delta H = -324{\cdot}04 \text{ kcal. mole}^{-1}$$

The most recent was made in 1947 by Wheeler, Whittaker, and Pike[3] who measured the heat of explosion of ethyl nitrate in a closed bomb in the absence of air; the quantity they measured, described as a "calorific value," corresponds to the equation:

$$\text{EtO·NO}_2\text{(l)} \longrightarrow 0{\cdot}5\text{N}_2 + (1+x)\text{CO} + (1-x)\text{CO}_2 + (2{\cdot}5-x)\text{H}_2 + x\text{H}_2\text{O(l)};\ \Delta U = -77{\cdot}6 \text{ kcal. mole}^{-1}$$

where x has a value between 0 and 1 which depends on the extent of the water-gas reactions. This possible variation in x affects the derived enthalpy of formation of ethyl nitrate by only 0·1 kcal. mole^{-1}.

Table 1. *Experimental values (kcal. mole^{-1}) for the enthalpy of formation at 25° of ethyl nitrate.*

Investigator	Experimental quantity measured	Result (kcal. mole^{-1})	Enthalpy of formation (kcal. mole^{-1}) Liquid	Gas
Berthelot	Esterification of liquid	6·2	−45·6	*−36·9* *
Thomsen	Combustion of vapour	324·04	*−43·6* *	−34·9
Wheeler, Whittaker, and Pike	Explosion of liquid (constant vol.)	77·6	−45·9	*−37·2* *

* Figures in italics are derived from the new latent-heat data.

There are no other primary determinations. For a commentary on the confusion surrounding the various values in standard compilations see the report of Hurwitz and Laidler.[4]

When these experimental results are combined with modern thermochemical data[5] the three values for the enthalpy of formation listed in Table 1 are derived.

Two of these figures apply to the liquid and one to the gas. To correlate them and assess their reliability accurate latent-heat data at 25° are necessary. Although there are

[1] See Berthelot, "Explosives and their Power," translated by Hake and Macnab, John Murray, London, 1892, p. 279.
[2] Thomsen, "Thermochemische Untersuchungen," Barth, Leipzig, 1886, Vol. IV; *Z. phys. Chem.*, 1905, **52**, 343.
[3] Wheeler, Whittaker, and Pike, *J. Inst. Fuel*, 1947, **20**, 137.
[4] Hurwitz and Laidler, Naval Ordnance Contract 10,260, Report CU/P/54.3.
[5] "Selected Values of Chemical Thermodynamic Properties," Nat. Bur. Stand. Circular 500, U.S. Dept. of Commerce, Washington, D.C., 1952.

vapour-pressure measurements by Goodeve,[6] at low temperatures (−80° to +20°) these are not accurate enough to give more than a mean latent heat of vaporization at −30°. Accordingly measurements have been made of the vapour pressure of ethyl nitrate from 0° to 68° and the Clausius–Clapeyron equation used to derive a value for the latent heat of vaporization at 25°.

Discussion.—When the Clausius–Clapeyron equation is applied to the vapour-pressure data the enthalpy of vaporization at 25° is found to be 8·7 kcal. mole^{-1}. This value has been used in conjunction with the primary experimental data to compare the values for the enthalpy of formation of gaseous and liquid ethyl nitrate. In Table 1 figures in italics are those obtained by means of the new latent-heat data.

It will be seen that Berthelot's determination agrees very well with that of Wheeler, Whittaker, and Pike: Thomsen's result is (numerically) lower. In the past numerous corrections—of which the most notable is that of Kharasch [7] who altered Thomsen's thermometer readings to the hydrogen scale—have been made to Thomsen's combustion figures. From Thomsen's data Kharasch derives for ΔH_f° $EtNO_3$(l) the value −45·2 kcal. mole^{-1}. Other authorities take other values.

In assessing the merits of the three figures and of their various emended values an important factor is the actual magnitude of the experimental measurement. Thus Berthelot's measurement of 6·2 kcal. mole^{-1}, even if in error by 5%, would lead to an error in heat of formation of only between 0·5 and 1% (0·3 kcal. in 45 kcal.). For Wheeler, Whittaker, and Pike's measurements to achieve the same final accuracy their "calorific value" of 77 kcal. must be correct to 0·5%; this is within the limits of modern calorimetry though the authors estimate conservatively an error of about 1%. At the other extreme is Thomsen's value of 324 for the heat of combustion. This needs to be known to 0·1% to reach the same standard of accuracy and however much Thomsen's data of 1886 are corrected they are unlikely to produce a figure as reliable as the other two.

Accordingly we have adopted the values listed in Table 2 for the standard thermodynamic properties of ethyl nitrate. Entropy and free energy figures are based on the low-temperature calorimetry by Gray and Smith.[8]

TABLE 2. *Principal chemical thermodynamic properties of ethyl nitrate.*

Enthalpy of formation at 25° of liquid	−45·7 kcal. mole^{-1}
,, ,, ,, gas	−37·0 ,,
Latent heat (ΔH_v) of vaporization at 25°	8·7 ,,
,, ,, ,, b. p.	8·1 ,,
Entropy (relative to absolute zero) at 25° of liquid	59·08 cal. deg.$^{-1}$ mole^{-1}
Entropy of formation at 25° of liquid	−118·1 ,, ,,
Gibbs free energy of formation (ΔF_f°) at 25° of liquid	−10·5 kcal. mole^{-1}

EXPERIMENTAL

Materials.—Pure ethyl nitrate supplied by the Explosives Research and Development Establishment, Waltham Abbey, was dried ($CaCl_2$) and fractionally distilled.

Apparatus and Method.—Standard apparatus was used for measuring vapour pressures. A bulb containing the sample of ethyl nitrate was connected to a mercury manometer. The liquid was frozen and the air was removed. The bulb and manometer were immersed in a water-bath. The height of the mercury was measured by a cathetometer. Allowance was made for the variation in density of the mercury.

TABLE 3. *Vapour pressure of ethyl nitrate. Interpolated values of vapour pressure from 0° to 60°.*

Temp. (c)	0·0°	10·0°	20·0°	30·0°	40·0°	50·0°	60·0°
Vapour pressure (mm. Hg)	16·3	29·2	49·9	81·8	129	197	292

Results.—Vapour pressure. Over a hundred readings of vapour pressure and temperature were taken between 20° and 68°. Readings were also made between 0° and 20° to overlap with Goodeve's data.[6] Table 3 gives some interpolated values at 10° intervals. The results obtained

[6] J. W. Goodeve, *Trans. Faraday Soc.*, 1934, **30**, 501.
[7] Kharasch, *J. Res. Nat. Bur. Stand.*, 1929, **2**, 359.
[8] Gray and Smith, *J.*, 1954, 769.

in the range 0—20° coincide with those of Goodeve, who derives the expression $\log_{10} p$ (mm.) = 8·57 − 2010/T° K and thus the effective temperature range extends down to −80°. Additional points above the range of vapour-pressure measurement made here are provided by b. p. data. At 728·4 mm. the b. p.[9] is 86·2°. At 760 mm. the b. p. is 87·7° (Timmermans and Mattaar[10] give 88·7° ± 0·1°; Perkin[11] gives 87·5—87·7°; Lecat[12] gives 87·68°). When all these results are represented as a graph of log p against 1/T° K a curved line results, indicating departure from the approximate relation log $p = A + B/T$. All the data are fitted by the Antoine equation $\log_{10} p$ (mm. Hg) = 7·035 − 1278/(t° C + 219·3°) (which has three empircal constants instead of two).

Latent Heat of Vaporization. The Clausius–Clapeyron equation, $dp/dT = \Delta H_v/T\Delta V$, may be used in its approximate form d ln p/dT = $\Delta H_v/RT^2$ to derive the latent heat of vaporization from the vapour-pressure equation, if the vapour is assumed to behave as a perfect gas. The uncertainty introduced by this assumption is probably less than 0·1 kcal. mole^{-1}. At 25°, ΔH_v = 8·7 kcal. mole^{-1}. At the normal b. p., ΔH_v = 8·1 kcal. mole^{-1}. The temperature variation of the latent heat may be conveniently represented over the temperature range −80° to +80° by the approximate expression ΔH_v (kcal. mole^{-1}) = 8·9$_5$ − t° c/100. Application to this expression of Kirchoff's equation, dΔH_v/dT = C_p (gas) − C_p (liquid), yields C_p (gas) − C_p (liquid) = −10 cal. deg.$^{-1}$ mole^{-1}. The specific heat of the liquid has been measured,[9] and at 25° is 40·7 cal. deg.$^{-1}$ mole^{-1}. Thus at this temperature C_p (gas) is approximately 31 cal. deg.$^{-1}$ mole^{-1}. Of this quantity 23 cal. deg.$^{-1}$ mole^{-1} arise from internal motions (vibrations and internal rotations). The ethyl nitrate molecule contains eleven atoms and is not linear, so that if all the possible vibrations are active they will contribute (3 × 11 − 6)R = 53·6 cal. deg.$^{-1}$ mole^{-1} to the specific heat. Therefore the temperature variation of the latent heat of vaporization suggests that at room temperature about one half of the possible vibrations of gaseous ethyl nitrate are active.

Entropy of vaporization. From these figures the standard entropy of vaporization (cal. deg.$^{-1}$ mole^{-1}) at the b. p. (Trouton's constant) is 22. This is much more satisfactory than that of 26 calculated by Goodeve from her low-temperature results.

We are grateful to Professor Laidler and Mr. Hurwitz of Washington for helpful discussions. We also thank Gonville and Caius College and the D.S.I.R. for the award of a research studentship and a maintenance allowance (to M. W. T. P.).

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University of Cambridge. [*Received, August 16th*, 1955.]

[9] Kopp, *Annalen*, 1856, **98**, 367.
[10] Timmermans and Mattaar, *Bull. Soc. chim. belges*, 1921, **30**, 218.
[11] Perkin, *J.*, 1889, **55**, 680.
[12] Lecat, *Ann. Soc. sci. Bruxelles*, 1927, I, **47**, 153.

40. *Naphthyridines. Part III.* Hydroxynaphthyridines.*

By E. P. Hart.

Nitration and bromination of 2- and 4-hydroxy-1 : 5-naphthyridine have afforded mononitro- and monobromo-derivatives in which by analogies the substituent is regarded as being at position 3. The structure of 4-hydroxy-3-nitro-1 : 5-naphthyridine has been proved by unambiguous synthesis.

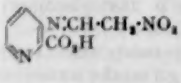
Substitution in the nucleus in hydroxynaphthyridines has been but little studied. No instance of halogenation has been described, and only one of nitration.[1] In the present work nitration of 2- and 4-hydroxy-1 : 5-naphthyridine with fuming nitric and sulphuric acids has given mononitro-derivatives. Likewise bromination in aqueous solution gave monobromo-derivatives, though perbromides are formed in alcohol or carbon tetrachloride. The substituting group in the above derivatives is regarded as being at position 3 by analogy

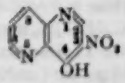
* Part II, *J.*, 1954, 4030.

[1] Mangini, *Boll. sci. Fac. Chim. ind. Bologna*, 1940, 165; *Chem. Zentr.*, 1940, II, 2613; *Chem. Abs.*, 1942, **36**, 5476.

with the corresponding products from hydroxy-pyridines and -quinolines,[2] and the structure of 4-hydroxy-3-nitro-1 : 5-naphthyridine (II) has been established by synthesis.

Several workers [3] have synthesised 4-hydroxy-3-nitroquinolines by reaction of methazonic acid with anthranilic acids, with subsequent cyclisation of the intermediate nitroethylideneamino-compounds. Schofield and Theobald [4] applied this reaction also to the formation of 4-aryl-3-nitroquinolines. With anthranilic acids use of acetic anhydride–sodium acetate was essential for the cyclisation; even then yields were only fair. 3-Aminopyridine-2-carboxylic acid and aqueous methazonic acid gave 3-2′-nitroethylideneaminopyridine-2-carboxylic acid (I) which, when heated in this cyclising medium, afforded 4-hydroxy-3-nitro-1 : 5-naphthyridine (II), identical with the compound obtained by direct nitration of 4-hydroxy-1 : 5-naphthyridine.

(I) 

 (II)

The hydroxynaphthyridines required were obtained by Skraup reactions from amino-hydroxypyridines. 3-Amino-4-hydroxypyridine gave 4-hydroxy-1 : 5-naphthyridine (see Part I [5]); 5-amino-2-hydroxypyridine has previously been obtained, as a red gum, by Petrow and Sturgeon,[6] who reduced 2-hydroxy-5-nitropyridine with iron in acidulated water; in the present work hydrogenation of the nitro-base over palladised charcoal has given a much cleaner product, which is extremely sensitive to oxidation. The overall yield of 2-hydroxy-1 : 5-naphthyridine from 2-hydroxy-5-nitropyridine has been raised by this method to 57%.

Experimental

5-Amino-2-hydroxypyridine.—2-Hydroxy-5-nitropyridine [7] (2 g.), suspended in methano (150 ml.), was hydrogenated in the presences of 10% palladised charcoal (2 g.). After the theoretical volume of hydrogen had been absorbed (2 hr.) the yellow solution was filtered rapidly, and evaporated under reduced pressure. Colourless crystals of the amino-base separated but were extremely sensitive to oxidation and could not be further purified. The dibenzoyl derivative crystallised from aqueous alcohol, m. p. 217°. Petrow and Sturgeon [6] record m. p. 218·5°.

2-Hydroxy-1 : 5-naphthyridine.—The preceding amino-base (from 2 g. of nitro-base), arsenic acid (2 g.), glycerol (4 g.), and concentrated sulphuric acid (6 ml.) were heated to 165°. After the initial violent ebullition had ceased, the temperature was kept thereat for 1 hr., the melt was extracted with dilute hydrochloric acid (2 × 30 ml.), and the extract concentrated to low volume and basified with ammonia solution. The precipitated solids were recrystallised (charcoal) from aqueous alcohol, giving 2-hydroxy-1 : 5-naphthyridine (1·2 g., 57% based on nitro-base) as colourless needles, m. p. 256°.

Hydroxynitronaphthyridines.—(*a*) 2-Hydroxy-1 : 5-naphthyridine (0·3 g.) was heated with nitric acid (*d* 1·5; 3 ml.) and 20% oleum (3 ml.) on the water-bath for 4 hr. Pouring the cooled mixture into a small volume of water gave yellow-orange crystals. Recrystallisation from aqueous alcohol afforded orange *2-hydroxy-3-nitro-1 : 5-naphthyridine* (0·25 g.), m. p. 272—274° (Found: C, 50·1; H, 2·8; N, 21·7. $C_8H_5O_3N_3$ requires C, 50·4; H, 2·6; N, 22·0%).

(*b*) 4-Hydroxy-1 : 5-naphthyridine (0·3 g.), nitrated as above, gave no precipitate in water. The solution was basified with solid sodium hydrogen carbonate and evaporated to dryness, and the residue extracted with hot alcohol (2 × 25 ml.). Concentration of this extract gave yellow *4-hydroxy-3-nitro-1 : 5-naphthyridine*, m. p. 328—330° (decomp.) (Found: C, 50·2; H, 2·5; N, 21·7%).

Bromohydroxynaphthyridines.—(*a*) To 2-hydroxy-1 : 5-naphthyridine (0·2 g.), dissolved in warm water (5 ml.), was added dropwise saturated bromine water until no further precipitate

[2] Binz and Maier-Bode, *Angew. Chem.*, 1936, **49**, 486; Bishop, Cavell, and Chapman, *J.*, 1952, 439; Koenigs and Geigy, *Ber.*, 1884, **17**, 589; Koenigs and Fulde, *Ber.*, 1927, **60**, 2107; Crowe, *J.*, 1925, 2028; Riegel, Lappin, Albisetti, Adelson, Dodson, Ginger, and Baker, *J. Amer. Chem. Soc.*, 1946, **68**, 1229.
[3] Colonna, *Gazzetta*, 1937, **67**, 46; 1939, **69**, 684; Musajo, *ibid.*, 1937, **67**, 222.
[4] Schofield and Theobald, *J.*, 1950, 395.
[5] Hart, *J.*, 1954, 1879.
[6] Petrow and Sturgeon, *J.*, 1949, 1157.
[7] Caldwell and Kornfeld, *J. Amer. Chem. Soc.*, 1942, **64**, 1696.

formed. Pouring the product into dilute sodium carbonate solution gave **3-*bromo*-2-*hydroxy*-1 : 5-*naphthyridine*** (0·22 g.) which crystallised from water as colourless needles, m. p. 295—297° (Found : C, 42·7; H, 2·0; N, 12·5; Br, 35·2. $C_8H_5ON_2Br$ requires C, 42·8; H, 2·2; N, 12·5; Br, 35·6%).

(*b*) 4-Hydroxy-1 : 5-naphthyridine (0·2 g.) similarly afforded **3-*bromo*-4-*hydroxy*-1 : 5-*naphthyridine*** (0·2 g.), m. p. 318° (decomp.) (from much water) (Found : C, 43·0; H, 2·3; N, 12·2; Br, 35·6%).

3-2′-Nitroethylideneaminopyridine-2-carboxylic Acid.—To a solution of 3-aminopyridine-2-carboxylic acid [prepared from quinolinimide [6] (10 g.)], acidified with hydrochloric acid (5 ml.), was added dropwise, with stirring, a solution of potassium methazonate [prepared from nitromethane (5 g.) and 50% aqueous potassium hydroxide (10 ml.)]. After a short time a heavy crystalline precipitate formed, which on recrystallisation from aqueous alcohol (charcoal) afforded the colourless ***nitroethylideneamino-compound***, m. p. 255° (decomp.) (Found : C, 45·8; H, 3·5; N, 20·3. $C_8H_7O_4N_3$ requires C, 46·0; H, 3·4; N, 20·2%).

4-Hydroxy-3-nitro-1 : 5-naphthyridine.—The preceding compound (1 g.) was heated with acetic anhydride (10 g.) and anhydrous sodium acetate (1 g.) on the water-bath until dissolution was complete, and then at the b. p. for 1 hr. No precipitate was formed either on cooling or pouring into water; the solution was basified with sodium hydrogen carbonate, and extracted continuously with ether. Evaporation of the dried (Na_2SO_4) extract gave yellow crystals. Crystallisation from a small volume of alcohol gave 4-hydroxy-3-nitro-1 : 5-naphthyridine, m. p. and mixed m. p. 328—330° (decomp.) (Found : C, 50·2; H, 2·5%).

I am indebted to Dr. E. Tittensor for his interest and advice.

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[*Received, August 30th,* 1955.]

[6] Sucharda, *Ber.*, 1925, **58**, 1728.

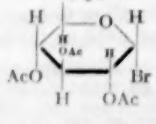
NOTES.

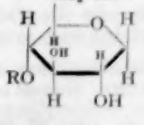
41. *Catalytic Reduction of Acetobromo-sugars.*

By L. ZERVAS and MISS C. ZIOUDROU.

FISCHER and ZACH (*Sitzungsber. kgl. preuss. Akad. Wiss.*, 1913, **16**, 311; *Chem. Zentr.*, 1913, I, 1668) attempted to synthesise an anhydrohexitol by the zinc dust reduction of tetra-*O*-acetyl-α-D-glucosyl bromide (I), but obtained glucal instead. We have found that the anhydrohexitol is obtained by catalytic hydrogenation with palladium as catalyst, in the presence of a tertiary base such as triethylamine or 4-ethylmorpholine. After removal of the acetyl groups, polygalitol (II*a*) was obtained, identical with that from various *Polygala* species (Piccard, *Bull. Soc. Chim. biol.*, 1927, **9**, 692; Shinoda, Sato, and Sato, *Ber.*, 1932, **65**, 1219; Freudenberg and Rogers, *J. Amer. Chem. Soc.*, 1937, **59**, 1602). The previous (Richtmyer, Carr, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 1477) and this new synthesis further support the formulation of polygalitol as 1 : 5-anhydro-D-sorbitol (Freudenberg and Rogers, *loc. cit.*; Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 64).

(I)





(II) *a* : R = H
b : R = $C_6H_{11}O_5$

The tertiary base could hydrolyse the tetra-*O*-acetylglucosyl bromide to tetra-*O*-acetylglucose, form a trialkylglycosylammonium salt, or eliminate hydrogen bromide to form tetra-*O*-acetyl-2-hydroxyglucal. If the last compound had been formed in large amount,

the main product of the catalytic reduction would have been styracitol, 1 : 5-anhydro-D-mannitol (Zervas, *Ber.*, 1930, **63**, 1689). Therefore, in order to slow down the rates of the above side reactions, the reduction was carried out in dilute anhydrous solution containing the theoretical amount of tertiary base and with a relatively large amount of catalyst.

Other acetobromo-sugars can also be reduced by this procedure. Thus, hepta-*O*-acetylcellobiosyl bromide gave finally 1 : 5-anhydro-4-(β-D-glucopyranosyl)-D-sorbitol (II*b*).

Experimental.—**1 : 5-*Anhydro*-D-*sorbitol*** (polygalitol). To the solution of 4·1 g. (0·01 mole) 2 : 3 : 4 : 6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (4·1 g., 0·01 mole) in anhydrous ethyl acetate (80 ml.), triethylamine (1 g., 0·01 mole) was added and the mixture was immediately hydrogenated in the presence of 0·5 g. of freshly prepared palladium black. Depending on the catalyst activity the hydrogenation was complete in 60—90 min., when 250 ml. of hydrogen had been absorbed (26°/756 mm.). The filtrate was twice washed with water and evaporated to dryness *in vacuo*. The syrupy residue, mainly consisting of polygalitol tetra-acetate mixed with a small quantity of tetra-acetylglucosyl bromide and other products, was treated with N-alcoholic potassium hydroxide (50 ml.) for 4 hr. at room temperature. Then, 2N-sulphuric acid (25 ml.) was added and the mixture was evaporated to dryness *in vacuo*. The residue was repeatedly extracted with absolute methanol and the combined filtrates were evaporated to dryness *in vacuo*. Complete removal of the inorganic salts was ensured by dissolving the residue in absolute methanol and concentrating the filtered solution to a few ml. At 0°, 0·65 g. (40%) of polygalitol separated, having m. p. 142—143°, $[\alpha]_D^{20}$ +42·1° (*c* 1·5 in H_2O) (Found : C, 43·75; H, 7·1. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·4%). Freudenberg and Rogers (*loc. cit.*) gave m. p. 142—143°, $[\alpha]_D$ +42·8—45°; Richtmyer, Carr, and Hudson (*loc. cit.*) gave m. p. 140—141°, $[\alpha]_D$ +42·4°.

Acetylation with acetic anhydride–pyridine gave polygalitol tetra-acetate, m. p. 75°, in almost quantitative yield (Richtmyer, Carr, and Hudson, *loc. cit.*, gave m. p. 73—74°).

1 : 5-*Anhydro*-4-(β-D-*glucopyranosyl*)-D-*sorbitol*.—Hepta-*O*-acetylcellobiosyl bromide (7 g., 0·01 mole) in ethyl acetate in the presence of triethylamine (1 g.) was catalytically hydrogenated as described above. Evaporation of the filtrate to dryness and recrystallisation of the residue from ethanol gave hepta-*O*-acetyl-1 : 5-anhydro-4-(β-D-glucopyranosyl)-D-sorbitol (4·5 g., 72%) as needles, m. p. 194°, $[\alpha]_D^{25}$ +4·6° (*c*, 10 in $CHCl_3$) (Fletcher and Hudson, *J. Amer. Chem. Soc.*, 1948, **70**, 310, gave m. p. 194—195°, $[\alpha]_D$ +4°).

Hydrolysis by Fletcher and Hudson's procedure (*loc. cit.*) afforded 1 : 5-anhydro-4-(β-D-glucopyranosyl)-D-sorbitol (85%), m. p. 172°, $[\alpha]_D^{25}$ +29·5° (*c* 4 in H_2O) (Found : C, 44·3; H, 6·9. Calc. for $C_{12}H_{22}O_{10}$: C, 44·3; H, 6·8%). Fletcher and Hudson (*loc. cit.*) and Maurer and Ploetner (*Ber.*, 1931, **64**, 281) gave m. p. 172°, 173°, $[\alpha]_D$ +29°, 29·3° (in H_2O).

This investigation was supported by a grant from the Rockefeller Foundation whom we thank.

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42. Rauwolfia *Alkaloids. Part I. Reserpine and Ajmaline from* Rauwolfia natalensis *Sond.* (R. caffra).

By BRUNO O. G. SCHULER and F. L. WARREN.

Rauwolfia natalensis Sond. (*R. caffra*), which is locally known as the quinine tree, is used medically by the Bantu. The Zulus use extracts for skin rashes, and the Pondos employ the bark for intestinal disorders.

Juritz (*Report Sen. Analyst, Cape Good Hope*, 1901, 58) reported the isolation of a bitter alkaloid, m. p. 200°, from a plant which he finally characterised as *R. natalensis* (*S. African J. Sci.*, 1914, **11**, 110). Rindl and Grôenewoud (*Proc. Roy. Soc. S. Africa*, 1932, **21**, 55) re-investigated *R. caffra* but isolated only amorphous alkaloidal material, one portion of which gave a perchlorate as needles (not analysed), m. p. 110—113°.

In view of the interest in this species we have re-investigated *R. caffra*. The aerial bark gave only small quantities of alkaloid which was intractable. Extraction of the root

bark in the cold by the elegant method of Djerassi, Gorman, Nussbaum, and Reynoso (*J. Amer. Chem. Soc.*, 1954, **76**, 4463) gave reserpine, m. p. 262—263°, in small quantities. The main alkaloid, m. p. 158—161°, was identified as ajmaline by its colour reactions with ferric chloride and nitric acid (cf. Anet, Chakravarti, Robinson, and Schlittler, *J.*, 1954, 1246), and by the comparison of its properties and those of its derivatives with those reported by Siddiqui and Siddiqui (*J. Indian Chem. Soc.*, 1931, **8**, 667; 1932, **9**, 539; 1935, **12**, 37) and by Anet *et al.* (*loc. cit.*). This comparison is shown in the Table.

Isolated alkaloid compared with ajmaline.

	Anet *et al.*	Siddiqui	This paper
Ajmaline	158—160°	158—160°	158—161°
$[\alpha]_D$	+144 (anhyd.)	+198 (hydr.)	+128 (hydr.)
Hydrochloride (hydr.)	250 (cryst.)	253—255 (amorphous)	254 (cryst.)
Picrate (hydr.)	—	126—127	125
Picrate (anhyd.)	—	223	220
Oxime HCl	218	—	214—218

This alkaloid showed ultraviolet maxima at 250 and 292 mμ (log ε 3·95 and 3·55 respectively) and infrared bands at 3·00, 3·17, 3·5—4·00, and 6·21 μ. Absorption in these regions has been reported for ajmaline by Anet *et al.* (*loc. cit.*). In carbon tetrachloride absorption was also observed at 5·83 μ indicative of a carbonyl group as reported by Chatterjee and Bose (*Experientia*, 1953, **9**, 254): in agreement, however, with the observations by Anet *et al.* (*loc. cit.*) we were unable to detect this band when the spectrum was measured in Nujol or chloroform. This band is broad and weak as might be expected from a dynamic carbinol–amine system envisaged in the Robinson–Schlittler (*loc. cit.*) formula.

The infrared spectrum in the skeletal region was identical with that of a specimen kindly supplied by Dr. E. Schlittler of Ciba Pharmaceutical Products Inc. In spite of the difference in infrared spectrum in the different solvents, the spectra of ajmaline hydrochloride and of the freshly regenerated base were identical in the ultraviolet so that the ready isomerism observed by Skinner (*J.*, 1950, 823) for cotarnine and berberine does not exist.

Experimental.—Extraction. A mixture of ether (1·7 l.), benzene (500 ml.), and ethanol (200 ml.) was added to finely ground root bark (200 g.) of *R. caffra*, collected in March in the Pietermaritzburg district of Natal. After 15 min. 7N-ammonia (400 ml.) was added, the whole shaken for 2 days under nitrogen, and the solution filtered. The residue was extracted twice more by the same procedure. The combined extracts were evaporated at <35° under reduced pressure. The dry residue was extracted with benzene (2 × 100 ml.), and the benzene solution run through a column of alumina (75 g.; activity II). The benzene eluates gave a non-alkaloidal amorphous powder, m. p. 139°. Ether gave a gum, a methanol solution of which on evaporation gave rod-like crystals which were removed. The mother-liquor slowly deposited crystalline nodules.

The nodules, crystallised from methanol, gave reserpine (30 mg.), m. p. 262—263°, undepressed by specimen kindly supplied by Parke Davis, Detroit (Found: N, 4·5. Calc. for $C_{33}H_{40}O_9N_2$: N, 4·6%). Muller, Schlittler, and Bein (*Experientia*, 1952, **8**, 338) give m. p. 262—263°. The infrared spectra of the two samples were identical.

The rod-shaped crystals, crystallised from methanol, gave ajmaline as rectangular plates (1 g.), m. p. 158—161°, with previous swelling at 142° (Found: C, 70·4; H, 8·6; N, 7·8. Calc. for $C_{20}H_{26}O_3N_2.CH_4O$: C, 70·4; H, 8·4; N, 7·8%). Ajmaline hydrochloride, dried at 100° for 3 hr., had m. p. 254° (Found: C, 59·9; H, 7·3. Calc. for $C_{20}H_{26}O_3N_2,2HCl$: C, 60·1; H, 6·9%).

The authors acknowledge with thanks grants from the S.A.C.S.I.R. and the interest shown by Dr. W. S. Rapson, Director of the N.C.R.L., in these studies.

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43. *The Melting Point and Magnetic Susceptibility of Zinc Chloride.*

By D. A. Craw and J. L. Rogers.

During an investigation of thermodynamic properties of the copper–zinc system, pure anhydrous zinc chloride was required for use in alloy concentration cells. Published m. p.s of zinc chloride ranged from 239° (Lorenz and Michael, *Z. phys. Chem.*, 1928, **137**, *A*, 1) to 365° (Grünauer, *Z. anorg. Chem.*, 1904, **39**, *A*, 389); handbooks and textbooks generally quote figures between 262° and 290°. A reliable determination of the melting point was therefore necessary.

Experimental.—Dry hydrogen chloride was passed over pure mossy zinc at 410° and the slowly formed molten zinc chloride collected out of contact with the air in m. p. tubes. Initially the brass-block method was used to determine the m. p. as 318°, in close agreement with the reports by Biltz and Klemm (315° ± 3°; *Z. phys. Chem.*, 1924, **110**, 333) and of Klemm (318° ± 2°; *Z. anorg. Chem.*, 1926, **152**, 235).

The chloride was also prepared by a method due to Biltz and Klemm (*loc. cit.*) and Grünauer (*loc. cit.*), who, however, reported a considerably different m. p. Dry hydrogen chloride was passed through crystalline zinc chloride ("Anachemia" reagent grade) for 10 min., then the zinc chloride was heated slowly past its m. p. and dry hydrogen chloride was continuously bubbled through the melt at 350° for a further 45 min. Purified dry argon was exchanged for the hydrogen chloride gas and passed for 20 min. before the zinc chloride was transferred out of contact with the air to m. p. tubes. This method of dehydration was repeated several times with minor variations and a constant m. p. 318° ± 2° found (Found: Zn, 47·8; Cl, 52·0. Calc. for $ZnCl_2$: Zn, 48·0; Cl, 52·05%).

The m. p. for the latter preparation was determined in an apparatus similar to that described by White (*Analyt. Chem.*, 1947, **19**, 432). Hartwell (*ibid.*, 1948, **20**, 374), in an investigation of melting-bath liquids, recommended the use of a Silicone oil (General Electric 9981-LTNV-40) for the 300° region and this proved entirely satisfactory. Stem correction was made for the mercury-in-glass thermometer whose accuracy was checked by comparison with a Pt–Pt-13%Rh thermocouple previously calibrated at the f. p. of tin, lead, and zinc.

No workers have reproduced the m. p. obtained by Grünauer (365°); he gave no analysis of his product or temperature calibration, and it seems certain that this work was in error.

The magnetic susceptibility of zinc chloride (but not that of carefully dehydrated zinc chloride) has been measured previously, either with crystalline zinc chloride (Flordal and Frivold, *Ann. Physik*, 1935, **23**, 425) or in aqueous solution (Kido, *Sci. Reports Tohoku Univ.*, Ser. 1, 1932, **21**, 149; König, *Ann. Physik Chem.*, 1887, **31**, 273). The magnetic susceptibility of anhydrous zinc chloride was measured by one of us (J. L. R.) by a modified Gouy method (Henry and Rogers, to be published) and, the determined density of 2·79 ± 0·05 g./c.c. at 23° being used, the mass susceptibility was calculated as $-0{\cdot}47_7 \times 10^{-6} \pm 0{\cdot}010 \times 10^{-6}$ e.m.u. at 23°. If Flordal and Frivold's figure (*loc. cit.*) for the susceptibility of crystalline zinc chloride is corrected for the use of a different standard, it becomes $-0{\cdot}458 \times 10^{-6}$ e.m.u.

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44. *3- and 5-Ethyloctahydropyrrocolines.*

By K. S. N. Prasad and R. Raper.

Clemo [1] obtained, by the alkaline degradation of strychnine, a bicyclic base whose octahydro-derivative has the composition of an ethyl- or dimethyl-octahydropyrrocoline. Various bases of this type have been synthesised,[2] all of which differed from the reduced strychnine derivative. We have now synthesised 3- and 5-ethyloctahydropyrrocoline (I) and (II), neither of which is identical with the reduced base from the alkaloid.

Ethyl 2-piperidylacetate was condensed with ethyl α-bromobutyrate, and the product

[1] Clemo, *J.*, 1936, 1695.
[2] Clemo, Fox, and Raper, *J.*, 1953, 4173.

cyclised to a ketone which on reduction gave the 3-ethyl compound (I). 2 : 6-Lutidine was converted by means of formaldehyde into the alcohol. Dehydration and reduction of the resulting vinyl derivative gave 2-ethyl-6-methylpyridine which was converted into ethyl 6-ethyl-2-pyridylacetate by the usual method. This ester differed from the isomer,

(I) (II)

ethyl α-(6-methyl-2-pyridyl)propionate, made by methylation of the corresponding acetate. Hydrogenation of the 6-ethyl acetate, condensation of the resulting piperidine with ethyl bromoacetate, cyclisation, and reduction gave the 5-ethyl-pyrrocoline (II).

Experimental.—Ethyl α-2-(ethoxycarbonylmethyl)piperidinobutyrate. Ethyl 2-piperidylacetate [3] (5 g.), ethyl α-bromobutyrate (6·5 g.), and anhydrous potassium carbonate (5 g.) were heated at 100° with occasional stirring for 10 hr. Water was added and the oil taken up in ether, dried, and distilled. The *ester* (5 g.) had b. p. 140—145°/2 mm. (Found: C, 63·6; H, 9·7. $C_{15}H_{27}O_4N$ requires C, 63·2; H, 9·5%).

3-Ethyloctahydro-2-oxopyrrocoline.—The above diester (3 g.) in dry toluene (5 ml.) was added to powdered potassium (1 g.), suspended in toluene (5 ml.) cooled in ice. After the vigorous reaction was over the mixture was heated for 4 hr. (water-bath), alcohol was added to dissolve unchanged metal, followed by water (15 ml.) and concentrated hydrochloric acid (20 ml.). The solution was heated for 20 hr. (water-bath) and evaporated to dryness in a vacuum. The residue was basified (50% potassium hydroxide), and the *ketone* extracted with ether, dried, and distilled (1 g.; b. p. 120—125°/12 mm.) (Found: C, 71·7; H, 10·5. $C_{10}H_{17}ON$ requires C, 71·8; H, 10·2%). The *picrate*, from ethanol, has m. p. 165° (Found: C, 48·5; H, 5·5. $C_{10}H_{17}ON,C_6H_3O_7N_3$ requires C, 48·5; H, 5·1%).

3-Ethyloctahydropyrrocoline.—The ketone (0·8 g.), amalgamated zinc (5 g.), and concentrated hydrochloric acid (12 ml.), were set aside for 2 hr. and then refluxed for 24 hr. The decanted liquid was strongly basified (50% potassium hydroxide) and the *base* extracted with ether, dried, and distilled [0·35 g.; b. p. (bath temp.) 140—150°/12 mm.] (Found: N, 8·8. $C_{10}H_{19}N$ requires N, 9·1%). The *picrolonate*, from ethanol, has m. p. 140° (Found: C, 57·7; H, 6·8. $C_{10}H_{19}N,C_{10}H_8O_5N_4$ requires C, 57·5; H, 6·5%).

2-2′-Hydroxyethyl-6-methylpyridine. 2 : 6-Lutidine (64 g.) was converted into its lithium derivative [4] the ethereal solution of which was cooled in a freezing mixture, and formaldehyde from paraformaldehyde (40 g.) passed into it. After being stirred for 45 min. and refluxed for a similar period the product was decomposed with ice and hydrochloric acid, the ether layer removed, the aqueous layer basified (potassium hydroxide), and the *base* extracted with chloroform, dried (K_2CO_3), and distilled (25 g.; b. p. 120—125°/12 mm.) (Found: C, 69·85; H, 8·3. $C_8H_{11}ON$ requires C, 70·1; H, 8·0%). Its *picrate*, from ethanol–ether, has m. p. 97° (Found: C, 45·4; H, 3·8. $C_8H_{11}ON,C_6H_3O_7N_3$ requires C, 45·9; H, 3·8%). 2 : 6-Lutidine (20 g.) was recovered.

2-Methyl-6-vinylpyridine. The above alcohol (25 g.) was dehydrated with potassium hydroxide (10 g.) for 6 hr. at 100°/12 mm., the crude product distilling off. It was dried in ethereal solution (Na_2SO_4) and formed an *oil* (19 g.; b. p. 65—70°/12 mm.) (Found: C, 81·2; H, 7·9. C_8H_9N requires C, 80·7; H, 7·6%). Its *picrate*, from ethanol, has m. p. 163° (Found: C, 47·9; H, 3·7. $C_8H_9N,C_6H_3O_7N_3$ requires C, 48·2; H, 3·4%).

2-Ethyl-6-methylpyridine. The vinylpyridine (18 g.) was hydrogenated in ethanol (50 ml.), over palladised charcoal (3 g.; 5%) at 20° and atmospheric pressure, giving the *ethylpyridine* (16 g.; b. p. 68—73°/12 mm.) (Found: C, 79·5; H, 9·3. $C_8H_{11}N$ requires C, 79·3; H, 9·1%). The *picrate*, from ethanol, has m. p. 125° (Found: C, 48·0; H, 4·3. $C_8H_{11}N,C_6H_3O_7N_3$ requires C, 48·0; H, 4·0%).

Ethyl 6-ethyl-2-pyridylacetate. This was prepared from the above base (15 g.) by Woodward and Kornfeld's method.[4] Unchanged base (4 g.) and the *ester*, a pale yellow oil (7 g.; b. p. 134—137°/12 mm.), were obtained (Found: N, 7·6. $C_{11}H_{15}O_2N$ requires N, 7·3%). The *picrolonate*, from ethanol, has m. p. 157° (Found: C, 54·6; H, 5·0. $C_{11}H_{15}O_2N,C_{10}H_8O_5N_4$ requires C, 55·1; H, 5·0%).

[3] Clemo, Morgan, and Raper, *J.*, 1935, 1743.
[4] Woodward and Kornfeld, *Org. Synth.*, 1949, **29**, 44.

Ethyl 6-ethyl-2-piperidylacetate. This was obtained by hydrogenating the above ester (7 g.) in glacial acetic acid (30 ml.) over platinum oxide (0·1 g.) for 24 hr. at room temp. and 100 lb./sq. in. pressure, adding more catalyst (0·1 g.), and shaking the mixture a further 24 hr. The *ester* (6·5 g.) had b. p. 116—120°/12 mm. (Found: C, 65·8; H, 10·6. $C_{11}H_{21}O_2N$ requires C, 66·3; H, 10·6%).

Diethyl 6-ethylpiperidine-1 : 2-diacetate. Ethyl 6-ethyl-2-piperidylacetate (6 g.) and ethyl bromoacetate (6 g.) reacted, in presence of anhydrous potassium carbonate (as above), to give the *diacetate* (4·8 g.; b. p. 138—143°/2 mm.) (Found: C, 62·9; H, 9·7%).

5-Ethyloctahydro-2-oxopyrrocoline. The diacetate (3 g.), cyclised with the aid of potassium, and decarboxylated as described above, gave the *ketone* (1 g.; b. p. 118—123°/12 mm.) (Found: C, 71·3; H, 10·5%). The *picrate*, from ethyl acetate, has m. p. 158° (decomp.) (Found: C, 48·6; H, 5·3%).

5-Ethyloctahydropyrrocoline. When the 2-keto-derivative (0·5 g.) was reduced (Clemmensen) *5-ethyloctahydropyrrocoline* [0·2 g.; b. p. 140—150° (bath temp.)] was obtained (Found: N, 8·9%). The *picrate*, from ethanol, has m. p. 175° (Found: C, 50·2; H, 5·7. $C_{10}H_{19}N,C_6H_3O_7N_3$ requires C, 50·3; H, 5·8%).

Ethyl α-(6-methyl-2-pyridyl)propionate. Ethyl 6-methyl-2-pyridylacetate[5] (5·5 g.) was treated with powdered potassium (1·2 g.) in ether (60 ml.). Methyl iodide (4·4 g.) was carefully added to the potassium derivative, and the whole refluxed 10 hr. Water (20 ml.) was added, and the *ester* extracted with ether, dried, and distilled (3·6 g.; b. p. 120—123°/4 mm.) (Found: N, 7·5%). The picrolonate, from alcohol, has m. p. 170° (Found: C, 55·0; H, 5·2%).

KING'S COLLEGE, NEWCASTLE UPON TYNE, 1. [*Received, July 29th*, 1955.]

[5] Clemo, Fox, and Raper, *J.*, 1954, 2693.

45. *Crystalline 2 : 3-Di-O-methyl-β-D-xylose.*

By ERIC G. MEEK.

SYRUPY 2 : 3-di-*O*-methyl-D-xylose was first isolated from the hydrolysate of methylated esparto xylan by Hampton, Haworth, and Hirst (*J.*, 1929, 1739). Chanda, Hirst, Jones, and Percival (*J.*, 1950, 1289) also obtained it from the same source; after two years their specimen crystallised in the α-form, and had m. p. 79—80°, $[\alpha]_D^{18}$ +70° (3 min.), +23° (14 hr., constant) (*c* 1·0 in H_2O) (Chanda, Percival, and Percival, *J.*, 1952, 260). Hirst, Percival, and Wylam (*J.*, 1954, 189), and Aspinall and Mohamed (*J.*, 1954, 1731), have also isolated this ether in the α-form.

The β-isomer of 2 : 3-di-*O*-methyl-D-xylose has now been obtained despite the fact that the syrupy ether was seeded with Chanda, Percival, and Percival's α-crystals.

The α- and the β-isomer have the same m. p., but this was depressed on admixture: they gave different *X*-ray powder photographs and different infrared spectra. All attempts to obtain more α-crystals have been unsuccessful; syrups left unseeded, or seeded with α- or β-crystals have either remained syrupy or given β-crystals.

Experimental.—All rotations were measured in 1 dm. tubes. Zero time was taken to be the time of addition of the solvent: dissolution was usually complete in 3—5 min.

Hydrolysis of a methylated wheat-straw xylan, and cellulose column chromatography yielded syrupy 2 : 3-di-*O*-methyl-D-xylose which was characterised as its aniline derivative and as 2 : 3-di-*O*-methyl-D-xylonamide. The syrup was seeded with Chanda, Percival, and Percival's α-crystals; crystallisation was almost complete in two weeks. After draining on porous tile to remove traces of syrup the *β-form* had m. p. 79—80° (mixed m. p. with Chanda, Percival, and Percival's sample 65—67°), $[\alpha]_D^{20}$ −7·3° (5 min.), +4·4° (10 min.), +13·8° (15 min.), +24·2° (25 min.), +26·7° (35 min., constant) (*c* 2·0 in H_2O); $[\alpha]_D^{20}$ −30·3° (10 min.), −23·0° (30 min.), −9·9° (70 min.), −0·5° (110 min.), +9·9° (190 min.), +14·9° (280 min.), +18·1° (380 min., constant) [*c* 2·2 in EtOH–H_2O (4 : 1)] (Found: C, 46·7; H, 7·8; OMe, 34·6. $C_7H_{14}O_5$ requires C, 47·2; H, 7·9; OMe, 34·8%).

Chanda, Percival, and Percival's crystals had $[\alpha]_D^{18}$ +40·6° (10 min.), +36·0° (30 min.), +29·0° (75 min.), +24·6° (115 min.), +17·4° (220 min.), +14·5° (320 min.), +12·6° (585 min., constant) [*c* 2·1 in EtOH–H_2O (4 : 1)].

In view of the very rapid initial changes in rotation, even in aqueous ethanol, Hudson's rule could not be applied with accuracy.

Dr. S. A. Barker of Birmingham University kindly examined these samples and reported: "Both specimens showed very similar spectra over a wide range with only slight changes in wave number. However, the most striking difference was that the α-form had two peaks, at 1230 and 736 cm.$^{-1}$, not present in the β-form. The latter is due to symmetrical ring breathing frequency and has been found in all other derivatives of xylose in the α-form, but never in the β-form" (cf. Barker, Bourne, Stephens, and Whiffen, *J.*, 1954, 3468).

X-Ray powder photographs were taken by courtesy of Dr. C. A. Beevers with a Raymax tube with a copper target. The heavier lines given by both samples lay in the same region but had different spacings and intensities, thus indicating different crystal structures. The crystalline sample of 2 : 3-di-*O*-methyl-D-xylose obtained by Aspinall and Mohamed (*loc. cit.*) gave a photograph identical with that given by Chanda, Percival, and Percival's α-isomer.

The author thanks Professor E. L. Hirst, F.R.S., Dr. G. O. Aspinall, and Dr. E. Percival for helpful advice, and the British Rayon Research Association for the award of a Fellowship.

CHEMISTRY DEPARTMENT, THE UNIVERSITY, EDINBURGH. [*Received, August 3rd*, 1955.]

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46. *Carbohydrates of the Roots of the Parsnip*, Pastinaca sativa.

By D. M. W. ANDERSON and C. T. GREENWOOD.

DURING the isolation of starch from parsnips, *Pastinaca sativa*, other polysaccharides present in the roots were separated by successive extractions with cold water, hot water, cold 5% sodium hydroxide, and hot 5% sodium hydroxide. Results of analyses of the fractions obtained are shown in the Table.

Analyses of fractions isolated from parsnip roots (% of dry weight).

Fraction	Yield	Ash *	Protein †	Uronic acid anhydride	Polysaccharide ‡	Sugars obtained on hydrolysis §						
						Gal	G	M	A	X	R	F
P1 (cold water sediment)	28	0·4	37·1	8·8	53·7	1·3	46·2	0	4·9	0·8	0·6	0
P2 (,, extract)	20	17·4	24·2	7·4	51·0	11·2	24·4	0	12·8	1·6	0	1·0
P3 (hot water ,,)	13	6·6	6·2	41·5	45·7	6·0	17·6	0	17·0	1·4	3·7	0
P4 (cold NaOH ,,)	14	7·5	13·4	23·4	55·7	13·2	5·1	3·4	26·2	5·6	2·2	0
P5 (hot ,, ,,)	5	7·4	5·5	45·3	40·8	9·2	3·2	2·9	23·4	1·6	0·4	0
P6 (residue) *	11	3·1	0	2·2	12·7	0·8	9·1	0	0·9	2·0	0	0

* Not sulphated. † %N × 6·25.

‡ Hydrolysable non-acidic polysaccharide (calculated by difference).

§ Hydrolysis conditions: 2% H_2SO_4 in a sealed tube at 98° for 7 hr.

Chromatographic conditions: butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3; top layer) solvent phase; 48 hr. development time; aniline oxalate spray for aldoses; urea oxalate for ketoses; estimations by Somogyi's reagent.

Gal = galactose; G = glucose; M = mannose; A = arabinose; X = xylose; R = rhamnose; F = fructose.

* This fraction was only 18% hydrolysed under these conditions (see text).

Examination of the unhydrolysed cold water extract (P2) by chromatography indicated that raffinose, sucrose, glucose, and fructose were present as free sugars, together comprising about 2% of the fraction. No polyfructosans were detected. No free sugars were present in any of the other fractions. Hydrolysis of fractions P1, P3, P4, and P5 liberated a sugar which behaved chromatographically as rhamnose. Rhamnose may, however, be readily confused with D(+)-apiose under these conditions, and the latter has been shown to exist in other members of the *Umbelliferae*.[1] Comparison with authentic D(+)-apiose (kindly placed at our disposal by Dr. D. J. Bell) established that the sugar was in fact rhamnose. The presence of this sugar in plant materials is not unusual.[2] Fraction (P6) was only 18% hydrolysed under the conditions described, but the residue on treatment with 72% sulphuric

[1] Bell, Isherwood, Hardwick, and Cahn, *J.*, 1954, 3702.

[2] Cf. Hirst, *J.*, 1949, 522.

acid gave 95% of glucose together with traces of xylose, and was therefore cellulosic material, (2% of lignin remained).

Traces only of alkali-soluble mannan exist, and surprisingly little xylan is present. The uronic acid content of all fractions is high, however, and the roots provide a good source of pectic material and also of araban. The starch (from P1) in unusual in that potentiometric titrations with iodine have shown it to contain only 11·1% of amylose,[3] and this material is being investigated in detail

Experimental.—Before analysis, samples were dried at 80° *in vacuo* for several hours. Solutions were concentrated under reduced pressure at 40°. Percentages of nitrogen were determined by duplicate semi-micro Kjeldahl determinations, whilst estimations of uronic acid anhydride were made by McCready's method.[4]

Extraction of roots. (*a*) Removal of oil. Parsnips were peeled, minced, and then exhaustively extracted by successive treatments with boiling methanol, methanol–benzene (2 : 1 v/v), and ether (Found, on defatted material: ash, 3·02; protein, 16·2; uronic acid anhydride, 22·4%).

(*b*) Extractions with water. Defatted roots (55 g.) were extracted with cold water (8 × 300 ml.; each 3 min.) in an "Atomix" blender. Each extract was filtered through muslin to yield on centrifugation a protein-contaminated starch (P1) and supernatant liquors. The latter when reduced in valume and freeze-dried yielded the cold-water extract (P2). The residual material was similarly extracted with water at 98°, and the polysaccharides isolated by freeze-drying to yield fraction (P3).

(*c*) Extractions with alkali. The residue was vigorously stirred with 5% sodium hydroxide (w/v : 8 × 200 ml.; each 1 hr.) at room temperature, and then at 98°. In each case the alkaline extract after centrifugation was brought to pH7 with acetic acid. The volume was then reduced, salts were removed by dialysis for 96 hr., and the fractions (P4 and P5, respectively) were isolated by freeze-drying. The final residue was washed free from alkali and dried (P6).

The overall yield was 91% of the dry weight of original material.

Analysis of fractions. Qualitative and quantitative estimations of the sugars liberated on hydrolysis were carried out as previously described,[5] with the exception that separation of arabinose from mannose in fractions P4 and P5 was achieved by use of ethyl acetate–acetic acid–water (3 : 1 : 3 v/v; non-aqueous phase) as solvent.[6]

With the exception of fructose (which is about 35% decomposed), the liberated sugars were stable under the hydrolysis conditions used (see Wylam [6]). (Since fructosans were absent, the appearance of fructose in hydrolysed P2 was only supplementary to the results obtained from a study of the unhydrolysed cold-water extract.) A weighed amount of ribose was added to each fraction (preliminary experiments having shown this sugar to be absent from all hydrolysates) to permit estimation of losses during analysis. In each case, the total weight of sugars found was between 75 and 90% of the expected quantities. Values quoted in the table have been corrected, the loss for each sugar being assumed to be proportionate to the actual weight found.

Although uronic acids were present in all hydrolysates (naphtharesorcinol test), no attempt was made to separate them chromatographically.

Confirmation of the presence of rhamnose. The acid hydrolysates of fractions P1, P3, P4, and P5 were examined chromatographically without preliminary neutralization,[7] since apiose is extremely reactive to alkali.[1] The R_F value (0·24) of the suspected rhamnose and of an authentic sample of rhamnose was the same when duplicate chromatograms were run with (*a*) butan-1-ol saturated with water, and (*b*) butan-1-ol saturated with aqueous boric acid. The R_F value of authentic D(+)-apiose was 0·26 for (*a*), but only 0·04 in (*b*). This showed that the sugar present was rhamnose, not apiose.

Department of Chemistry, University of Edinburgh. [*Received, August 23rd*, 1955.]

[3] Anderson and Greenwood, *J.*, 1955, 3016.
[4] McCready, Swenson, and Maclay, *Analyt. Chem.*, 1946, **18**, 290.
[5] Anderson and Greenwood, *J. Sci. Food Agric.*, 1955, **6**, 587.
[6] Jermyn and Isherwood, *Biochem. J.*, 1949, **44**, 402.
[7] Gaillard, *Nature*, 1953, **171**, 1160.
[8] Wylam, *J. Sci. Food Agric.*, 1954, **4**, 167.

47. *The Oxidation of Aromatic Primary Amines with Benzoyl Peroxide.*

By J. T. Edward.

The oxidation of *N*-substituted anilines with benzoyl peroxide affords *o*-benzamidophenols in yields of up to 40%.[1,2] However, only low yields of *o*-benzamidophenols have now been obtained from the following primary amines: *o*- and *m*-toluidine, 2 : 4 : 1- and 2 : 5 : 1-xylidine, *p*-bromo-, *p*-chloro-, and 2 : 4-dichloro-aniline. 2-Benzamido-5-bromo-, -5-chloro-, and -3 : 5-dichloro-phenols from the last three amines are new; the structures of the last two were proved by converting them into 6-chloro- and 4 : 6-dichloro-2-phenylbenzoxazole respectively. No phenol was isolated on oxidation of aniline, *p*-toluidine, 2 : 6 : 1-xylidine, *p*-anisidine, or 2 : 4 : 6-tribromoaniline.

The neutral and the basic fractions from these reactions were complex mixtures, from which the azo-compound and, in most instances, the *N*-arylbenzamide were obtained by chromatography on alumina. Smaller amounts of more complex coloured products were also separated by chromatography; their structures are being investigated.

The isolation of azobenzene and benzanilide from the reaction product of aniline with benzoyl peroxide has been reported by Horner and Schwenk.[3] The formation of *N*-arylbenzamides indicates that benzoyl peroxide, besides reacting with amines by a free-radical mechanism,[2,3] undergoes the heterolytic reaction: $Ar{\cdot}NH_2 + Bz_2O_2 \longrightarrow Ar{\cdot}NHBz + BzO_2H$.

Experimental.—Isolation of phenols. Oxidation of the amines by an equimolar amount of benzoyl peroxide in benzene solution at 5°, as judged by the heat evolution and extent of darkening of the solution, was usually complete in less than 10—20 min., although the solutions were usually kept at room temperatures for several hours. However, the less basic amines were oxidized slowly (cf. Horner and Scherf[4]); the solutions containing 2 : 4-dichloro- and 2 : 4 : 6-tribromo-aniline were refluxed for 2 and 6 hr. respectively. The solutions were extracted with sodium hydrogen carbonate to remove benzoic acid (65—80% yields), then with sodium hydroxide to remove phenol. The phenols, all crystallized from aqueous alcohol or acetone, are tabulated.

Amine oxidised *	Phenol *	Yield (%)	M. p. †	Formula		C (%)	H (%)
o-Toluidine	2-Benzamido-*m*-cresol	2	185° (189)[5]	$C_{14}H_{13}O_2N$	Found	74·1	5·7
					Calc.	74·0	5·7
m-Toluidine	2-Benzamido-*p*-cresol	<1	184 (191)[6]	—	—	—	—
2 : 4 : 1-Xylidine ...	2-Benzamido-3 : 5 : 1-xylenol	5	209—210 (211—212)[7]	—	—	—	—
2 : 5 : 1-Xylidine ...	2-Benzamido-3 : 6 : 1-xylenol	12	209—212 (210—211)[8]	$C_{15}H_{15}O_2N$	Found	74·8	6·3
					Calc.	74·7	6·2
p-Bromoaniline ...	2-*Benzamido-5-bromophenol*	5	241—242	$C_{13}H_{10}O_2NBr$	Found	53·9	3·5
					Reqd.	53·4	3·5
p-Chloroaniline ...	2-*Benzamido-5-chlorophenol*	6	231—232	$C_{13}H_{10}O_2NCl$	Found	63·2	3·8
					Reqd.	63·0	4·1
2 4-Dichloroaniline	2-*Benzamido-3 : 5-dichlorophenol*	7	167—170	$C_{13}H_9O_2NCl$	Found	55·8	3·3
					Reqd.	55·4	3·2

* NH_2 and OH = 1. † M. p.s in parentheses are from the literature.

6-Chloro-2-phenylbenzoxazole, sublimed from a mixture of equal parts of 2-benzamido-5-chlorophenol and phosphoric oxide heated to 230°/15 mm., crystallized from aqueous acetone as needles, m. p. 98—100° (Found: C, 68·0; H, 3·2. $C_{13}H_8ONCl$ requires C, 68·0; H, 3·5%).

[1] Gambarjan, *Ber.*, 1909, **42**, 4003.
[2] Edward, *J.*, 1954, 1464.
[3] Horner and Schwenk, *Annalen*, 1950, **566**, 69.
[4] Horner and Scherf, *ibid.*, 1951, **573**, 35.
[5] Gibson, *J.*, 1923, 1269.
[6] Von Auwers and Czerny, *Ber.*, 1898, **31**, 2692.
[7] Von Auwers and Borsche, *Ber.*, 1915, **48**, 1698.
[8] Von Auwers and Schornstein, *Fortschr. Chem. Phys. phys. Chem.*, 1924—1926, **18**, 42; *Chem. Zentr.*, 1924, II, 2269.

4 : 6-*Dichloro-2-phenylbenzoxazole*, prepared as above from 2-benzamido-3 : 5-dichlorophenol, crystallized from aqueous acetone in needles, m. p. 133—135° (Found : C, 59·9; H, 3·3. $C_{13}H_7ONCl_2$ requires C, 59·1; H, 2·7%).

Chromatographic separation of the neutral products. After removal of benzoic acid and phenols, the benzene solutions were dried (Na_2SO_4), concentrated at reduced pressure, and chromatographed on alumina. The column was developed with benzene containing increasing proportions of chloroform. The azo-compounds invariably were the first band. Yields were as follows : azobenzene, m. p. 66°, 20%; 2 : 2′-dimethylazobenzene, m. p. 51—53°, 12%; 3 : 3′-dimethylazobenzene, m. p. 53—54°, 21%; 4 : 4′-dimethylazobenzene, m. p. 141—142°, 5%; 2 : 2′ : 4 : 4′-tetramethylazobenzene, m. p. 124—126°, 14%; 2 : 2′ : 5 : 5′-tetramethylazobenzene, m. p. 115—117°, 14%; 2 : 2′ : 6 : 6′-*tetramethylazobenzene*, m. p. 46—47° (Found : C, 80·2; H, 7·6. $C_{16}H_{18}N_2$ requires C, 80·6; H, 7·6%), <1%; 4 : 4′-dichloroazobenzene, m. p. 186—187°, 15%; 2 : 2′ : 4 : 4′-tetrachloroazobenzene, m. p. 162—163°, 5%; 4 : 4′-dibromoazobenzene, m. p. 204—208° (Found : C, 42·7; H, 2·4. Calc. for $C_{12}H_8N_2Br_2$: C, 42·4; H, 2·4%), 5%; 2 : 2′ : 4 : 4′ : 6 : 6′-hexabromoazobenzene, m. p. 212—213°, 13%; 4 : 4′-dimethoxyazobenzene, m. p. 161—162°, 10%. The m. p.s and colours of the compounds, and the colours of their solutions in concentrated sulphuric acid, agreed reasonably well with those reported in the literature.

The following benzanilides were obtained on further elution of the chromatograms : benzanilide, m. p. 160—161°, 28%; benzo-*m*-toluidide, m. p. 125°, 4%; benzo-*p*-toluidide, m. p. 157—158°, 4%; benzo-2 : 4 : 1-xylidide, m. p. 185—187°, 2%; benzo-2 : 5 : 1-xylidide, m. p. 135°; *N*-benzoyl-*p*-chloroaniline, m. p. 190—191° (Found : C, 67·9; H, 4·1. Calc. for $C_{13}H_{10}ONCl$: C, 67·4; H, 4·4%), 5%; and -*p*-bromoaniline, m. p. 206—208° (Found : C, 56·5; H, 3·9. Calc. for $C_{13}H_{10}ONBr$: C, 56·5; H, 3·7%), 19%; and benzo-*p*-anisidide, m. p. 153—154°.

Grateful acknowledgment is made to Professor M. Stacey, F.R.S., for constant encouragement and to this University for an Imperial Chemical Industries Limited Research Fellowship.

Chemistry Department, The University, Birmingham. [*Received, September 16th*, 1955.]

OBITUARY NOTICE.

WILLIAM GODDEN.

1884—1954.

WILLIAM GODDEN was born in Canterbury on December 31st, 1884, and died in Aberdeen on September 3rd, 1954. He was educated at the Simon Langton School, Canterbury, and at the Royal College of Science, graduating in 1907 with the degree of B.Sc.

His first appointment was as clinical analyst to the late Dr. F. W. Pavy, F.R.S., who specialised in the dietary treatment of diabetes. Godden assisted him in his research in carbohydrate metabolism at the South Kensington Physiological Laboratory of the University of London.

After Pavy's death, Godden joined the staff of the Department of Agricultural Chemistry at the University of Leeds in 1912 and was Senior Assistant to Professor Charles Crowther. His interest in animal nutrition, already aroused by his work in London, now developed fully and continued to be his chief interest for the rest of his life.

In 1922, Godden joined the staff of the then recently created Rowett Research Institute, as head of the Biochemistry Department in succession to Dr. R. H. A. Plimmer, who had moved to the Chair of Biochemistry at St. Thomas's Hospital, London. During the first years Godden spent at the Institute, he was primarily engaged in research on mineral metabolism and this henceforward became the branch of nutrition that held his special interest. His scientific contributions were many and important and they covered a wide range of problems. At first, he gave his attention to determining the variation in the mineral content of feedingstuffs, mainly herbage; to studying some of the causes of this variation; and to measuring the influence of dietary changes and the physiological state of the animal on its ability to absorb and retain minerals. Later, his interests broadened to include studies of the blood changes provoked by diets badly balanced in their mineral content and of the depletion and replenishment of skeletal reserves of minerals.

The scope of the work he directed in his department went well beyond the bounds of mineral metabolism, embracing research in proteins and vitamins and the utilisation of dietary energy. Throughout his own work and in his direction of the work of others, he remained primarily a chemist, with unremitting emphasis on the supreme importance of accuracy in all analytical work.

From 1930, when the first of the long series of dietary surveys undertaken by the Rowett Research Institute was made, Godden was almost continuously active with help and advice. He had foods, of which the composition was not known, analysed in his laboratory; he organised and helped to make analyses of the field data. In particular, he helped both in the original planning of the field work and in the interim and final analyses of the material accumulated over years in the major survey sponsored by the Carnegie United Kingdom Trust, the report of which was issued early in 1955. During the war he bore many heavy responsibilities that fell on him in the *ad hoc* projects which arose from the need for more efficient livestock production. Largely as a result of this and his insistence on taking a share of civil defence duties, his health began to fail and continued indifferent until the time of his death.

After the war, his responsibilities grew no lighter for, as Deputy Director of the Institute, he had an important part to play in the great expansion of the Institute's work and staff, laboratory facilities and building programme. To this he devoted his full energy and skill. After retiring in 1949, he joined the staff of the Commonwealth Bureau of Animal Nutrition and continued to give part-time, but most highly valued, scientific assistance up to his death.

William Godden's many friends here and abroad felt the deepest regret at his passing, but they could draw consolation from the knowledge that his lifelong interest in the science of animal nutrition, the activity of his mind, and his phenomenal memory of the scientific literature continued unimpaired to the last day he spent with his colleagues. He gave fully of his time and energy and our knowledge of animal nutrition is the richer thereby. He is survived by his son, Dr. W. J. Godden, of Dumfries. His wife, Emily Berrie, died on June 29th, 1955.

D. P. CUTHBERTSON.

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p-Hydroxy-azobenzene-p'-sulphonic acid	68/- D
m-Iodobenzotrifluoride (b. p. 177° C.)	31/- D
7-Iodo-8-hydroxyquinoline-5-sulphonic acid	31/- H
β-Lactose	8/- H
L-Lysine-*monohydrochloride* (95%)	56/- H
2-Methyl-5-chlorobenzimidazole (m. p. 205° C.)	90/- H
5-Nitrobenzotriazole	80/- H
p-Nitro-fluorobenzene	12/- D
1-Nitronaphthalene	11/- H
5-Nitronaphthalene-1-sulphonic acid	138/- D
Oxytocin (lyophilised) (2 Voegtlin units/mg.)	86/- G
Perfluoro-octanoic acid	34/- D
Phthalaldehyde acid (o-aldehydo-benzoic acid)	8/- D
Phthalazone	7/- D
Phthalonitrile (o-dicyanobenzene)	8/- D
Reductic acid (1 : 2-dihydroxycyclo-pentenone-3)	72/- D
Tetra-chloro-difluoroacetone ($CCl_2F{\cdot}CO{\cdot}CCl_2F$)	6/- D
Tetra-hydro-lavandulol	43/- H
Tetra-hydroxyethylenediamine	15/- H
Trichloro-trifluoroacetone ($CCl_2F{\cdot}CO{\cdot}CClF_2$)	6/- D

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Patent Applied For

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